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ABSTRACT

This curriculum module explores genes, environment, and human behavior. This book provides materials to teach about the nature and methods of studying human behavior, raise some of the ethical and public policy dilemmas emerging from the Human Genome Project, and provide professional development for teachers. An extensive Teacher Background section, including discussion of many new discoveries in the genetics of human behavior and the ethical, social, and legal implications, is included. The module also features five Classroom Activities with teacher pages, copymasters, and student pages. Contains 88 references. (WRM)

Genes,

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and

Human Behavior

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Genes, Environment, and Human Behavior

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**Evaluation Form for
Genes, Environment, and Human Behavior**

Your feedback is important. After you have used the module, please take a few minutes to complete and return this form to BSCS, Attn: HGN4, 5415 Mark Dabbling Blvd., Colorado Springs, CO 80918-3842.

1. Please evaluate the *Teacher Background* by marking this form and providing written comments or suggestions on a separate sheet.

Sections used	not helpful			very helpful	
Introduction	1	2	3	4	5
What Is Genetics?	1	2	3	4	5
What Is Behavior?	1	2	3	4	5
Methods and Assumptions of Research in Behavioral Genetics	1	2	3	4	5
Ethical, Legal, and Social Implications of Behavioral Genetics	1	2	3	4	5
Glossary	1	2	3	4	5

2. Please evaluate the *Classroom Activities* by marking this form and providing written comments or suggestions on a separate sheet. Rate the activities for their effectiveness at teaching concepts of behavioral genetics.

Activities used	not helpful			very helpful	
Activity 1: Investigating Complex Traits	1	2	3	4	5
Activity 2: Human Variation	1	2	3	4	5
Activity 3: A Novel Trait	1	2	3	4	5
Activity 4: Finding Genes That Influence Novelty-Seeking Behavior in Humans	1	2	3	4	5
Activity 4 Extension: Chi-Square Calculation	1	2	3	4	5
Activity 5: Paula's Law	1	2	3	4	5

3. What are the major strengths of this module?
4. What are the major weaknesses of this module?

5. Please rate the overall effectiveness of this module: not effective very effective
1 2 3 4 5

6. Please provide a description of the classes in which you used this module: (circle response)

College: 2 year 4 year High school: grade 9 10 11 12

freshman sophomore junior senior Level of class: basic honors 2nd year

How many students used the module? _____ How many students per class? _____

Ethnicity: approximate % of minorities: _____

Description of school: _____

College: liberal arts science High school: urban suburban rural

7. Have you used BSCS materials before? ☐ yes ☐ no

Have you used the first BSCS genome module, *Mapping and Sequencing the Human Genome: Science, Ethics, and Public Policy*? ☐ yes ☐ no

If yes, please provide feedback on a separate sheet that you think will help us if we revise that module.

Have you used the second BSCS genome module, *The Human Genome Project: Biology, Computers, and Privacy*? ☐ yes ☐ no

Have you used the third BSCS genome module, *The Puzzle of Inheritance: Genetics and the Methods of Science*? ☐ yes ☐ no

8. Please provide your name and contact information below:

Name _____

School _____

Mailing address _____ ☐ home ☐ work

Phone _____ ☐ home ☐ work

FAX _____ ☐ home ☐ work

E-mail address _____

Was the address on your mailing label for receipt of the module correct? ☐ yes ☐ no

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Teacher Background

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Introduction

Why was this module developed?

Among the many reasons for developing this module, BSCS found the following to be most compelling:

- to lead students away from thinking of human traits, normal and abnormal, as the result of single genes; in other words, to introduce students to the concept of multifactorial causation for the majority of human phenotypes;
- to reduce some of the anxiety related to understanding that behavioral characteristics have a genetic component by demonstrating that even for the traits that have been shown to have a high degree of heritability, that component rarely exceeds 50 percent; in other words, we remain, for the most part, in control of our behavior in spite of the genetic influences;
- to introduce teachers and students to some of the methods used to investigate the genetic components of behavior (in particular, twin and association studies), including their efficacy and their limitations;
- to improve understanding of the extremes of behavior through a clear presentation of the genetic and environmental components of normal behaviors that may lead to organic psychoses. This is a reversal of the classical approach to genetics research where investigation of rare genetic diseases was justified on the basis that the data so obtained would lead us to a better understanding of normal gene function;
- to help students understand why human populations are so genetically variable, how that vari-

ability arose, why it is important to our survival, and how our variability will serve to protect us as environments change in the future; and

- to raise some of the ethical and public-policy dilemmas emerging from modern studies in human genetics, especially the Human Genome Project, where funding has been available from the outset through the program dubbed "ELSI" to do research into the ethical, legal, and social issues associated with genetic research.



Figure 1.1 Members of the writing team: front row (left to right) Edward Drexler, Mary Ann Cutter, George Vogler; middle row (left to right) John Zola, Jeffrey Murray; back row (left to right) Joel Gelernter, Ronald Davidson, Laurence McCullough.

Finally, and perhaps most importantly, the dissection of the components of individual differences in behavioral traits, including personality, sexual orientation, tendencies toward alcoholism, and intelligence is almost endlessly fascinating. Moreover, behavioral genetics undoubtedly will play an important societal role in the design of public policy in the future, relying more on sound science than on the highly politicized and sometimes capricious rationales so prevalent today.

What background do students need to use this module?

To derive the greatest benefit from this module, BSCS suggests that students have a basic understanding of Mendelian inheritance and molecular genetics. Familiarity with the following topics is assumed:

- Mendel's laws of segregation and independent assortment;
- the chromosome theory of inheritance, including genetic linkage and recombination;
- the chemical nature of the gene, including the structure of DNA; and
- the central dogma, which states that genetic information resides in DNA, passes through an RNA intermediate, and is ultimately expressed as protein.

Student activities

This module introduces high school students to the concept that human behavior has genetic and environmental components. Genetic influence on human behavior, however, does not mean that any single gene causes behavior. There are no genes for sexuality, no genes for intelligence, no genes for alcoholism; there are no genes for any human behavior. Genes only provide the code for making things, and the things they make are polypeptides, which are simply chains of amino acids. (They also code for the various types of RNAs.) These chains of amino acids, under the influence of their own chemistry as well as the effects of intracellular environments, and later on, the environments of the organs and tissues in which they find themselves, twist and fold into three-dimensional structures. The function of a polypeptide is the result of its structure. Sometimes proteins combine polypeptide chains encoded by the same gene or its alleles, and sometimes with polypeptides from other genetic loci, to produce cell structures such as collagen or connective tissue.

Other polypeptides act as regulators of gene activity, turning specific genes or sections of chromosomes on and off, often at highly specific times during development. Many other polypeptides function as enzymes, the biological catalysts that control the myriad of biochemical reactions that are essential to life. Inevitably, complex traits arise from the brain, a complex organ that is itself the product of the interaction of many genes and environmental influences. Human behavior is unquestionably influenced by genes, and research is just beginning to uncover associations between specific genes and elements of behavior. The precise role of most of these genes remains, for the most part, enigmatic.

The five activities in this module introduce students to the complexity of the interactions of genetic, developmental, and environmental phenomena on human behaviors and help students realize that neither genes nor environment tells the whole story. Intelligence is used as an example of a complex human behavior, as is novelty-seeking behavior. The multifactorial nature of human behaviors is illustrated by comparing them to traits exhibiting Mendelian patterns and to a complex physical trait, adult height. The students learn to understand human behavior in terms of genes and environment, and they explore techniques used by behavioral geneticists. An important goal of the module is to develop among the students an appreciation of the potential impact of this emerging knowledge on public policy.

Conceptual Organization of the Activities. The five activities in the module are organized into a conceptual whole that introduces students to the meaning of human behavior, to types of variation in populations, to the study of behavioral genetics, and then to the methodology for isolating genes that influence behavior. The final activity draws on lessons learned from the previous activities and asks students to use information from behavioral genetics to set social policy.

Activity 1: Investigating Complex Traits. This activity engages students in the study of human behavior through the provocative (and fictitious) notion that a single gene is responsible for human intelligence. The activity serves as a review of Mendelian genetics and leads students to conclude that single-gene inheritance is inadequate to explain the variation in human intelligence.

Activity 2: Human Variation. Students model variation in human height as an example of a physical trait that exhibits a continuous distribution in the population. The activity introduces height as a multifactorial trait, meaning that it is influenced by genetic and environmental factors.

Activity 3: A Novel Trait. Novelty-seeking behavior is used to demonstrate that behavioral traits, like physical traits, also can display continuous distributions. The activity introduces the use of twin studies (a type of population study) in investigations of the genetic and environmental influences on behavior.

Activity 4: Finding the Genes That Influence Novelty-Seeking Behavior in Humans. This activity extends the idea that genes can contribute to behavior by introducing students to methods for identifying the genes themselves. Students continue their investigation into novelty-seeking behavior by modeling a gene association study that links a DNA polymorphism to the behavior. Despite the association, it is clear that the gene merely influences the behavioral variation in a population but does not determine the behavior.

Activity 4 Extension: Chi-Square Calculation. Linkage of a gene to a behavior is never clear-cut. The behavior itself is often difficult to define and methods for measuring it may be imprecise. Environmental influences are always significant and sometimes overshadow genetic influences. In this extension activity, students use the chi-square calculation to determine if the association of the genes identified in Activity 4 to novelty-seeking behavior is likely to be real or just due to chance.

Activity 5: Paula's Law. This final activity asks students to evaluate information from behavioral genetics to set social policy. The behavior in question is alcoholism. Legislation has been proposed that restricts the sale of alcoholic beverages based on an individual's genotype. This activity reinforces the lesson that individual behavior cannot be predicted from population studies, and it illustrates how behavioral genetics has implications for social policy.

Dealing with Values and Controversial Issues. Instructors sometimes feel that the discussion of value issues is not appropriate in the science class-

room or that it detracts from the learning of "real" science. This module, however, is based on the conviction that there is much to be gained by involving students in analyzing issues of science, technology, and society. Society expects all students to function as citizens in the democratic process, and their school experience should provide opportunities for them to learn how to deal with contentious issues with civility, objectivity, and fairness. Likewise, students need to learn that science affects life in many ways. Opportunities to consider some of these ways also will reinforce those scientific principles that we desire to teach.

The activities in this module provide opportunities for the students to discuss, interpret, and evaluate human behavioral genetic research in light of values and ethics. Many issues that students will encounter—especially the privacy of genetic information and related public-policy questions—are potentially controversial. How much controversy develops will depend on many factors, such as the degree of homogeneity that exists among your students with respect to socioeconomic status, perspectives, value systems, and religious preferences. It also will depend on how you handle your role as facilitator of the discussion. Your language and attitude may be the factors that are most important to the flow of ideas and the quality of exchange among the students.

Neutrality is probably the single most important characteristic of a successful discussion facilitator. The following behaviors will help you guide your students in discussions in which factual information is balanced with feelings.

- Encourage your students to discover as much information about the issue as possible, and ask questions that will help your students distinguish between those components of an idea or issue that scientific research can answer and those components that are a matter of values. Students should understand the importance of accurate information to any discussion and should recognize the importance of distinguishing factual information from opinions.
- Keep the discussion relevant and moving forward by questioning or posing appropriate problems or hypothetical situations. Invite your students to respond to or to build on each other's ideas. Avoid asking questions that have exact

answers unless the facts are important to the integrity of the discussion. Encourage everyone to contribute, but do not force reluctant students into the discussion.

- Use unbiased questioning to help the students critically examine all views presented. Help your students consider different points of view thoroughly by asking them to define the relevant arguments and counterarguments. Let the students help you promote the expression of alternative points of view.
- Allow for the discussion of all feelings and opinions. Avoid becoming a censor of views that are radical or shocking (as long as these views are consistent with the facts). When a student seems to be saying something for its shock value, look to see whether other students recognize the inappropriate comment and invite them to respond.
- Avoid seeking consensus on all issues. The multifaceted issues that the students discuss result in the presentation of divergent views, and students should learn that this is acceptable. In some cases, however, helping the group reach consensus on a compromise solution to a problem may demonstrate compromise as a powerful determinant of cooperative community action.
- Keep your own views out of the discussion. Experts in science education recommend that teachers withhold their personal opinions from students. The position of teacher carries with it an authority that might influence students. The danger also exists that the discussion might slip into indoctrination into a particular value position, rather than an exploration of divergent positions. Either result misses the point of the activities. If your students ask what you think, you may wish to respond with a statement such as, "My personal opinion is not important here. We want to consider your views."
- Acknowledge all contributions in the same even-handed manner. If the class senses that you favor one group of ideas over another, you will inhibit open debate and discussion. For example, avoid praising the substance of contributions. Instead, praise the willingness of students to contribute by making such comments as, "Thanks for that idea" or "Thanks for those comments." As you display an open attitude, a similarly accepting climate will begin to develop within the class.
- Emphasize that everyone must be open to hearing and considering diverse views. Point out that we cannot make intelligent decisions if we close ourselves off from some viewpoints. Even if we cannot agree with or are offended by a viewpoint, we still must hear it so that we know that it exists and can consider it as we shape our own views.
- Create a sense of freedom in the classroom. Remind students, however, that freedom implies the responsibility to exercise that freedom in ways that generate positive results for all. If necessary, remind them as well that there is a fine line between freedom and license. In general, freedom is a positive influence, while license usually generates negative results.
- Insist on a nonhostile environment in the classroom. Do not allow your students to make *ad hominem* arguments (arguments that attack the person instead of the idea). Help your students learn to respond to ideas instead of to the individuals presenting those ideas.
- Respect silence. Reflective discussions often are slow. If you break the silence, your students may allow you to dominate the discussion.
- Finally, at the end of the discussion, ask your students to summarize the points that they and their classmates have made. Let your students know that your respect for them does not depend on their opinion about some controversial issue. If students feel that they must respond in particular ways to gain your approval, your class will not discuss issues openly and with forthrightness.

Following those general suggestions should help you stimulate meaningful student-to-student interaction with as little direct involvement by you as possible. Initially, some students may have difficulty responding without specific direction. It is important, however, that you resist the temptation to intervene extensively in the initial, sometimes uncomfortable phase of long silences and faltering responses. Unless students are given opportunities to evaluate ideas and values in the context of a larger problem, they may never learn to do so.

Implementation Support. The following table will help you schedule teaching this module. It lists estimated times and materials required for each student activity.

Table I.1 Implementation Support

Activity	Estimated Time	Materials Required
Activity 1: <i>Investigating Complex Traits</i>	20–30 minutes	Copymaster 1.1, <i>Late Breaking News</i> overhead transparency of anonymous SAT or ACT scores (optional)
Activity 2: <i>Human Variation</i>	50 minutes	small colored beads plastic film canisters with hole in lids paper or plastic cups Copymaster 2.1, <i>Human Variation Worksheet—Female</i> Copymaster 2.2, <i>Human Variation Worksheet—Male</i> Copymaster 2.3, <i>Histogram Template for Heights</i> overhead transparency of Copymaster 2.4, <i>Modeling Genetic and Environmental Influences</i>
Activity 3: <i>A Novel Trait</i>	50–75 minutes	Copymaster 3.1, <i>Novelty-Seeking Survey</i> Copymaster 3.4, <i>Novelty-Seeking Score Data for Fraternal Twins</i> blank paper graph paper hat, bucket, or other opaque container overhead transparency of Copymaster 3.2, <i>Scatterplot of Novelty-Seeking Score Data for Identical Twins</i> overhead transparency of Copymaster 3.3, <i>Scatterplot of Height for Identical Twins</i> overhead transparency of Copymaster 3.5, <i>Scatterplot of Novelty-Seeking Score Data for Fraternal Twins</i> (optional)
Activity 4: <i>Finding the Genes That Influence Novelty-Seeking Behavior in Humans</i>	50 minutes	Copymasters 4.1–4.4, <i>Research Subjects: Genotypes and Novelty-Seeking Scores</i> Copymaster 4.5, <i>Gel Template Sheet</i> Copymaster 4.6, <i>Graph Template for Novelty-Seeking Score Data</i> Copymaster 4.7, <i>Histogram Template for Allelic Frequencies</i> hats, buckets, or other opaque containers extension materials (optional)
Activity 5: <i>Paula's Law</i>	50–75 minutes	Copymaster 5.1, <i>Reasons in Favor of and Against Paula's Law</i> Copymaster 5.2, <i>Applegate Genotype Results</i>

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What Is Genetics?

The discipline of genetics has been defined in a number of ways, including the narrow view that it is the science concerned with the passage of traits from parents to offspring. A more useful definition is the study of the heritable component of variability. The discipline began to take on some recognizable form with the great insights of the 19th-century biologists Charles Darwin and Gregor Mendel. Darwin realized that naturally occurring variation within and among species was the substrate upon which natural selection acted. The environment, of course, exerted the selective pressure. Mendel recognized that internal *factors*, the term he used for what we now know as genes, played a critical role in creating this natural variation. A living organism exists at the intersection of these two processes. Internal forces, the genes, constrain possible phenotypic variation among organisms, and largely autonomous external forces, the environment, mold the species on the basis of these internally proposed variations.

In the decades since these classical observations and conclusions, an almost metaphorical and rather pleasing picture unfolded: the environment poses problems and the organisms posit possible solutions from which the best (at the time) is usually chosen. In other words, the genes propose and the environment disposes. Genes, organisms, and environments interact so that each is both the cause and effect in a complex but increasingly analyzable way. Genes do not determine individuals, and environments do not determine species. At the level of the individual, genes do not act in a vacuum. They are subject to the ever-changing internal environment of the organism

(development), to the external forces of nature and the created milieu of societies (environment), and to elements of chance. There is no such thing as nature *versus* nurture; internal and external influences act simultaneously on organisms and species to shape them (nature *and* nurture). The result is the almost infinite variety of life that has fascinated biologists and anyone who has ever paused to think of who they are and how they might have gotten that way.

What is meant by single-gene inheritance?

This module is designed to help you and your students move away from the notion that Mendelian single-gene inheritance explains all of human genetics, either normal or abnormal. In addition, it is important to de-emphasize disease when dealing with human genetics in the classroom. That approach tends to perpetuate the mistaken notion that, like bacteria and viruses, our genes and chromosomes come to us to cause disease, pain, and pestilence.

Consider adult human height as a universal product of human inheritance. Growth can be measured with precision, but clearly we do not receive a height gene from each of our parents and split the difference to determine how tall we are. There are genes that specify a whole group of growth hormones, growth hormone receptors, as well as thyroid hormone and insulin, both of which have potent influences on growth. In addition, there are many genes that contribute to the length of bones. Furthermore, no matter what your genetic potential for growth happened to be, if you had experienced puberty

under near-starvation conditions, you likely would never have reached your genetic potential. The environment in which your genes are expressed also affects the shape of your face, the size of your nose, your gait, and many other physical characteristics. Now, consider a so-called classic single-gene defect, phenylketonuria or PKU. It is an autosomal recessive condition that results from a deficiency in the activity of a liver enzyme, phenylalanine hydroxylase. As a result of this deficiency, phenylalanine accumulates in the tissues and blood in amounts greater than usual. This excess induces alternate pathways of metabolism that dispose of phenylalanine, but some of the by-products of these rarely used pathways are toxic and cause tissue damage, including mental retardation. In addition, the block in metabolism leads to a deficiency of the metabolites of phenylalanine, one of which is melanin, the main pigment of the skin. Hence, children with untreated PKU have a pale complexion. Phenylalanine is also a precursor of serotonin, an important neurotransmitter, and this deficiency presumably further contributes to the intellectual handicap characteristic of PKU. Already we are seeing that many factors influence the phenotype of the disease, and we are just beginning.

Phenylalanine is an amino acid found in virtually all proteins, and its concentration in the fetus is maintained by the mother's relatively normal amounts of phenylalanine hydroxylase, which is active in her liver. When the PKU mutation is detected through newborn screening, which now is required in all fifty U.S. states and all of the Canadian provinces, as well as in many other countries around the world, a special diet low in protein, and especially controlled for

amounts of phenylalanine, can be instituted and the manifestations of the disease are usually prevented.

In spite of early detection and institution of the diet within the newborn period, there always has been a small handful of individuals who failed to respond to the diet and developed the various complications of PKU. Some of those cases were attributed to failure of the family to adhere to the strict diet with sufficient stringency and other cases to failure to start treatment early enough. Other so-called treatment failures, however, were due to mutations not in the phenylalanine hydroxylase gene itself but in genes associated with the metabolism of its co-factors. Co-factors for many enzymatic reactions are vitamins, and other enzymatic reactions are required to activate these co-factors. Inherited defects in those pathways can cause typical PKU symptoms, except that they are resistant to the diet therapy. Thus, here is a case where there is some *genetic* heterogeneity in the causation of a so-called single-gene defect.

There can be additional complicating factors. Consider the birth of an infant with PKU under near-starvation conditions. Quite possibly, the manifestations of PKU will never appear because the diet in such desperately poor circumstances may be so deficient in protein that levels of phenylalanine will never rise high enough to cause problems.

Thus, the single-gene defect of PKU is actually **multifactorial** (affected by genetic and environmental factors). The disease phenotype can depend on more than one genetic mutation, and the contributions of the environment are as essential to the development of the disease as to its prevention. The majority of Mendelian disorders fall into the multifactorial category, including the other popular example of autosomal recessive heredity, cystic fibrosis. More than six hundred different mutations in the gene responsible for CF have been described, and the correlation between the specific mutation and the phenotype is poor. In other words, we are unable, by and large, to predict the severity of the disease based on the exact mutation. Once again, manipulation of the environment in the form of various treatment modalities has changed the outcome of this disease dramatically.

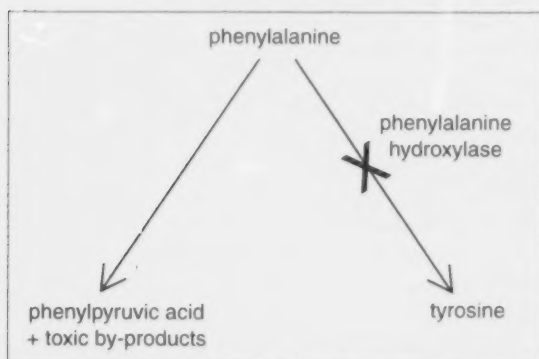


Figure T.1 In PKU, a lack of phenylalanine hydroxylase activity leads to the buildup of phenylalanine and toxic by-products.

The multifactorial nature of complex human diseases

The examples above should make it clear that nature and nurture act together in the development of

human characteristics. Presumably, some traits are largely genetic and influenced minimally, if at all, by the environment. Eye color is a good example, even though it is often used to illustrate single-gene inheritance. In general, brown eye color is thought to be dominant and blue recessive. How then does one explain green eye color, and hazel, and gray, and all the other shades seen in the human iris? Obviously, there are several additional alleles and probably more than one locus (gene) involved. It is even easier to observe the wide range in phenotypic variation in traits such as height, weight, arm length, intelligence, ability to throw a ball, susceptibility to illness, and others. In fact, most traits exhibit variation that is *continuous*, or smoothly distributed rather than *discrete*.

Research in recent years has revealed that many complex normal traits and common diseases are influenced by many genes. Such traits are said to be **polygenic**. Traits affected by many genetic and environmental factors are multifactorial traits. When multiple genes and/or environmental influences act together, their effects are seen as continuous distributions. Atherosclerosis, a complex disease of the heart, is influenced by genetic and environmental factors. Genes contributing to the metabolism of cholesterol, other blood lipids, and the regulation of platelet factors have been identified through biochemical and molecular approaches. Environmental factors that have been implicated include cigarette smoking and obesity, as well as some that are more controversial such as the involvement of the bacteria *Chlamydia pneumoniae*.

Cancer is influenced by genetics as well in that virtually all malignancies are associated with alterations of some type in the genetic material. Fortunately, several mutations must be present in the same cell at the same time in order for cancer to develop. The fact that cancer is genetic does not necessarily make a specific type of cancer hereditary; an environmental agent such as radiation can induce changes in the genetic material. One of the most common cancers, breast cancer, is under intense investigation from both the genetic and environmental points of view. Mutations in the genes *BRCA1* and *BRCA2* cause predispositions to malignancies of breast, ovary, prostate, and possibly other organs, but only varying proportions of those who inherit the mutations actually develop the cancer. Some will die before the disease has a chance to develop; for others, environmental "triggers" are

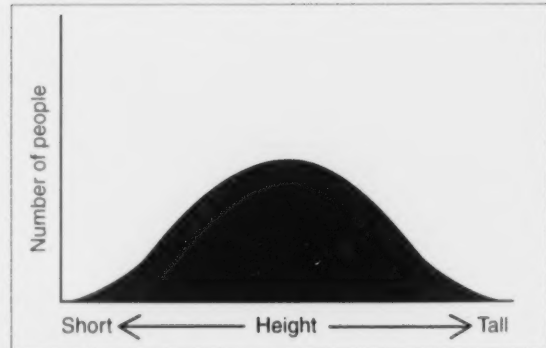


Figure T.2 Distribution of human heights showing the characteristic bell-shaped curve.

required. For the *BRCA* mutations, the environmental factors are just beginning to be proposed and studied, but they include such things as diet, radiation, and sex hormones. Finally, it should be noted that *BRCA* mutations account for only a small proportion of breast cancer cases.

Sources of genetic variation

The ultimate origin of all new genetic variability is, of course, recombination and mutation, phenomena that are, and always have been, a part of life. Without mutations, evolution never would have taken place at all. Only relatively unusual and major mutations, however, contribute to the development of new species; the vast majority are benign and simply contribute to variability. For example, as humans we have obvious similarities: two arms, two legs, one nose, one mouth, and so on. Nonetheless, despite these similarities, no two people look exactly alike. Even identical twins, who have the same DNA, have differences in the shapes of their faces and in how they metabolize specific substances. Most of this genetic variability can be attributed to the accumulation of mutations over the eons of the existence of life on this planet.

Recombination is a genetic mechanism that produces more genetic variation than could be achieved by simple independent assortment and transmission of whole chromosomes. Ordinarily, in sexual reproduction one inherits one chromosome from the mother and one from the father. Because of recombination during meiosis, however, the chromosome that is received from one parent is not the intact chromosome that the parent received from his or her mother or father, but rather a combination of both. This is because homologous versions of each

parental chromosome pair and exchange genetic material with each other. The result is that no transmitted chromosome is identical to a parental chromosome. If recombination did not occur, no new combinations of genes on a chromosome would result except through mutation.

Geneticists can use recombination frequencies to map the distances between genes. If a marker (a defined position on the chromosome) and a trait locus are on the same chromosome, the likelihood that recombination will separate them increases with distance. If a marker and a trait are never, or rarely, separated, they are said to be *linked*. The frequency of separation, therefore, depends on distance, which allows recombination to be used to measure genetic distance between a marker and a specific gene on the same chromosome. Thus, one of the primary mechanisms for introducing genetic variation into populations also can be exploited to study the genetic basis of variation itself.

In general, variability is a good thing. The more variable a species—that is, the greater the variation among a population of individuals in a species—the more likely that species is to survive in a changing environment. Of course, this advantage for the *population* affects specific individuals very little. In a sense, the price a species pays for the inherent variability that helps to ensure evolutionary success is the occasional deleterious mutation that sickens or kills an individual member.

Genetics and evolution

No overview of genetics, even so brief a treatment as presented here, is complete without a discussion of

the relationship between genetics and evolution, the conceptual thread that binds all of biology. Charles Darwin realized that variation among the members of any population of organisms is fuel for the fires of natural selection. In fact, Ernst Mayr asserts that one of Darwin's most important contributions was the firm establishment among biologists that a species is not composed of one fixed, identical type, but rather of unique individuals that differ from one another in a variety of ways. Furthermore, Darwin realized that the only variations that are important to natural selection and speciation are those that can be passed from generation to generation.

Darwin had a vexing problem, however: he could not define a valid mechanism by which variations could be transmitted unchanged from one generation to the next. The prevailing wisdom of the time—the mid- to late-19th century—was blending inheritance, the view that the characteristics of both parents blend together in the offspring, producing progeny that are intermediate in character between the two parents. Fleeming Jenkin, an engineer, argued in the 1860s that blending inheritance would make differential selection impossible because all members of a population would be the same. Furthermore, within a few generations, blending inheritance would mitigate the effects of any new variations that arose.

Darwin, who published *The Origin of Species* in 1859, could have found substantial help in the work of his contemporary, Gregor Mendel, who published his paper "Experiments in Plant-Hybridization" in 1865. Although Mendel almost certainly was aware of Darwin's work, most historians of science agree

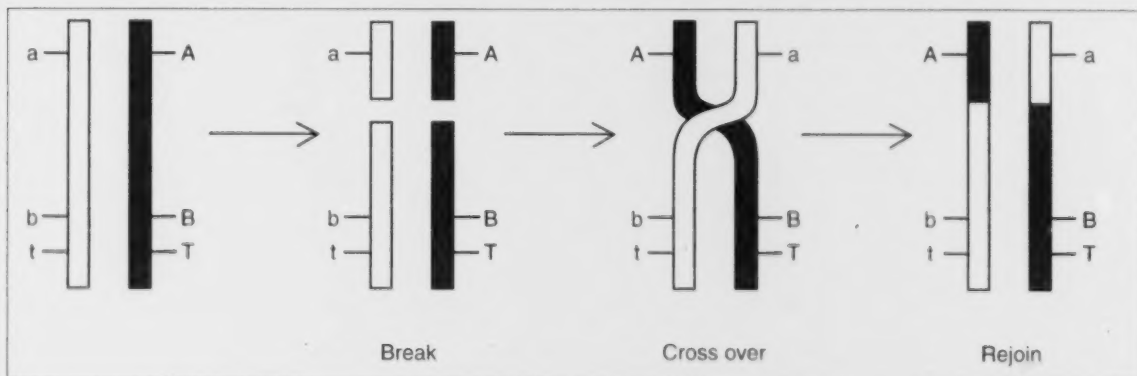


Figure T.3 Genetic marker A becomes separated from the trait (T) as a result of recombination, while marker B, located close to T, is rarely separated from the trait. Marker B is described as being linked to the trait.



Figure T.4 Charles Darwin at age forty from a portrait painted by J.F. Maguire.

that Darwin never read Mendel's paper, for had he done so, he likely would have recognized that Mendel's experiments provided solutions to his nagging problem. Mendel had demonstrated the particulate nature of inheritance, showing that hereditary information is carried by some discrete factors in the germ cells. Those discrete factors permit the transmission of traits in unchanged form. We now call those factors genes.

Ironically, the rediscovery of Mendel's work in 1900 (about two decades after Darwin's death) caused serious problems for Darwin's theory. As evolutionary biologist Douglas Futuyma (1986) explains, biologists of that era "dismissed continuous variation among individuals as inconsequential and largely nongenetic, and emphasized the role of discontinuous variants that displayed Mendelian ratios and clearly particulate inheritance." In 1918, however, Ronald A. Fisher found supporting evidence for Nilsson-Ehle's proposition that many traits are caused by multiple genes. Fisher showed that continuous variation (height, for example) results from multiple genes that are inherited in Mendelian fashion and that have small, additive effects.

The growth of population genetics and its accompanying mathematical models led to the Modern

Synthesis of Evolution during the 1930s and 1940s. This reconciliation of Mendel and Darwin involved some of this century's greatest biologists, among them Sewall Wright, J.B.S. Haldane, Ronald Fisher, Ernst Mayr, George Gaylord Simpson, Theodosius Dobzhansky, and G. Ledyard Stebbins.

The 1944 discovery by Avery, McCarty, and MacLeod that DNA is the genetic material and the 1953 delineation of DNA's structure by Watson, Crick, Wilkins, and Franklin provided additional opportunities to investigate genetic aspects of organic evolution, including the causes, rates, and effects of mutation. One obvious and current example of the relationship between genetics and evolutionary biology is the ability to compare DNA base sequences among species to help establish phylogenetic relationships.

In summary, the growth of genetics and the growth of evolution theory are intimately related. Because genetics is the study of the root source of biological variation, which is central to evolutionary mechanisms, an understanding of basic principles in genetics is central to an understanding of evolution itself.

The history of behavioral genetics

We chose behavioral genetics as the topic of this module for a variety of reasons. The activities show that human behavior is unquestionably multifactorial and should help lead students away from the overly simplistic thinking associated with single-gene, Mendelian patterns of inheritance. In addition, the controversial nature of the issues should intrigue the students. Reports of genes for homosexuality, violence, and intelligence, to mention just a few behaviors, have been filling the media with both factually correct and sometimes almost unbelievably misinterpreted data and conclusions. We also must



Figure T.5 Is a dimple a genetic trait? Kirk Douglas and his son Michael. A dimple is a complex physical trait that has genetic influences.

try to counteract any tendency that students may have to think deterministically about genetics and behavior, which is inherently unsettling to a human psyche that wants to believe that it has complete control over its fate.

The emergence of behavioral genetics as a legitimate subject for scientific study has been slow, at least until recently. Some of the reasons include the following:

- Often behavioral phenotypes are complex and difficult to define. For example, what is happiness; how does one define novelty seeking; and what constitutes aggression? Is homosexual behavior defined by one's thoughts and fantasies or merely actions? How sad must one be to be clinically depressed? All of those behaviors are complex and many constitute a continuum from normal to pathological. Defining the transition point always has been a difficult and contentious process.
- Adding to the complexity of defining phenotypes is the phenomenon of human neoteny, the remarkable prolongation of the stages of growth and development, including cognitive organization, far beyond intrauterine life. Insects, for example, emerge from the egg developmentally ready for an independent life. In sharp contrast, humans at birth have barely started development.

Although at first blush that may seem a dreadful handicap to the species, it is really a gift. The delay allows development of the nervous system to proceed in harmony with not only the intrauterine environment, where the fetus is protected from the outside, but also with the external environment, which provides unprotected sensory input, such as light, smells, and sounds, to which the neonate must adapt. Thus, we may be born with relatively little cognitive development hard wired in our brains, but that allows life experiences to mold our brains and to extend our opportunities for developmental variation. Ultimately, our post-delivery development allows learning for much longer periods of time than for any other primate. Neoteny, however, does complicate the separation of genetic and environmental contributions to behavior.

- Brain plasticity, which is a characteristic of neoteny, is another attribute of human development that complicates our understanding of behavioral phenotypes. Our brains contain billions of cells

that are dividing, migrating, differentiating, aggregating, producing networks, and undergoing programmed cell death. With so much happening, there is bound to be some noise, some randomness in the system. For example, a neuron may rotate in a certain direction or grow a fraction of a millimeter too long and thus make a connection not specifically programmed by the genes. In other words, chance is adding its two cents worth to variation. To the extent that this sort of plasticity occurs in the brain, it probably accounts for some of the differences in behavior, intelligence, and many other characteristics that have been documented in identical twins.

- Few genetic markers have been identified as causing behavioral abnormalities. As a result, starting points for research have not been available. It is important to understand that many of the genes that affect behavioral abnormalities have little or nothing to do with normal behavior. For example, the gene mutation that causes PKU, which has among its manifestations serious intellectual handicap and other behavioral abnormalities, has not led us to a gene that contributes to normal intelligence and behavior. As mentioned previously, the problem in PKU is in the *liver*, where an inborn error of metabolism causes the accumulation of toxic products and deficiencies of essential metabolites. Collectively and indirectly, these phenomena adversely affect the function of the brain.
- The study of behavioral genetics has been ignored partly because of the fear by scientists, the public, and funding agencies that results may lead to discrimination. For example, when a disproportionate number of males imprisoned for crimes of violence, including sexual assault, were found to carry an extra Y chromosome (the 47,XYY male), some researchers postulated that the extra Y chromosome might predispose men to these behavioral aberrations. To confirm the cause/effect hypothesis, it was essential to determine the incidence of 47,XYY males in the general population. The ideal approach would be to survey unselected, consecutively born newborn males with two goals in mind: first, to determine the incidence of 47,XYY males in the general population, and second, to follow the 47,XYY males periodically over many years to find out whether there would be any increased tendency to violence or sexual assaults or any other aggressive behaviors.

Several studies were initiated in the United States and other countries, but most of them were stopped early on because of the fear of stigmatization and of provoking a self-fulfilling prophecy. Anonymity, by the time the studies were started, had become impossible because of the widespread media attention to the 47,XYY chromosome "problem." The surviving studies lasted many years and contained relatively small sample sizes. They demonstrated that the extra Y chromosome indeed may have created a small predisposition to aggression, though the effect may have had more to do with the finding that 47,XYY males were on average slightly less intelligent than their 46,XY counterparts. More interesting, however, was the finding that the environment is far more important than genetics in influencing aggressive behavior. Virtually all the 47,XYY males imprisoned for crimes of violence came from extremely deprived social situations. The incidence of 47,XYY males in the general population is about 1/1000 male births, and the vast majority of those men have no more aggressive tendencies than their 46,XY counterparts.

- There are inhibiting traditions from education. Curriculum developers and teachers typically pay little attention to the biological variability among individual organisms. Thus, students are not accustomed to thinking about individual variation among experimental animals or students in the classroom. Activities are geared to the average of populations, often with failure to take into account even such obvious variables as sex differences. Learners with problems tend to be viewed as deviant rather than variant; emphasis is directed to weaknesses rather than concentrating on strengths.
- Finally, one of the major impediments to establishing the legitimacy of behavioral genetics in humans has been the unfortunate history that marred the beginnings of the field, the eugenics movement.

Francis Galton (1822–1911), Charles Darwin's half-cousin, is credited with initiating the field of behavior genetics. He coined the term eugenics, which means "well born," and in his book *Heritable Genius*, he showed that outstanding men often were aggregated within families. Curiously, women were never mentioned. One cannot help but wonder why it did not occur to Galton that these superior qualities could not have been transmitted without women.

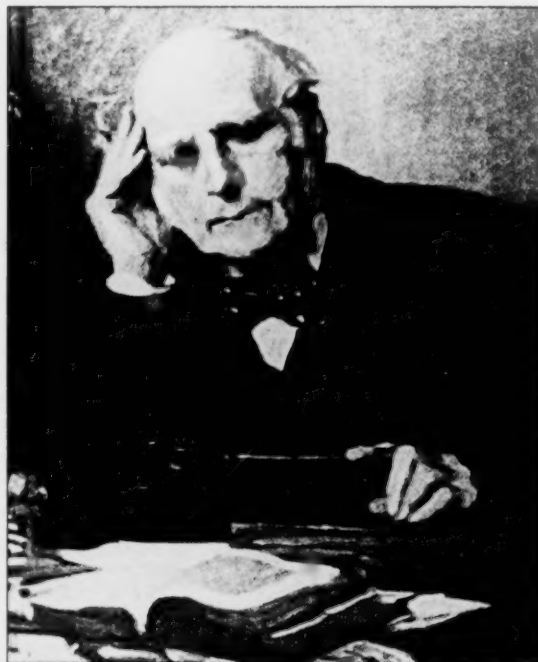


Figure T.6 Francis Galton, the father of the eugenics movement, also introduced the use of fingerprints for identification.

Another surprising feature of Galton's writings is the conclusion that these strong intrafamilial correlations were hereditary—that is, he ignored the possible power of living together, the effects of parental behavior, the influences of other members of the family, and socioeconomic status.

In the early 20th century, eugenicists focused on possible genetic causes for mental disabilities, among which they included mental retardation, alcoholism, criminality, and immorality. They were moved to worry about the crowding of poor houses, orphanages, jails, and asylums, noting that their rising populations were disproportionately made up of offspring of the poor and otherwise disadvantaged. Further studies indicated that the lower classes were having disproportionately greater numbers of children, and on the basis of some sloppy genetic investigations, early researchers drew some devastating conclusions, including such notions that intellectually "inferior" parents had even more seriously intellectually handicapped children. They also deduced that insanity was expressed usually when predisposing genes were inherited from both parents, as if the condition were

autosomal recessive and relatively uniform in cause. This "insight" led to such recommendations that individuals from families with a history of mental handicap should not marry or have children.

Prior to World War I, a Eugenics Record Office was established at the Cold Spring Harbor Laboratory, where Charles Davenport was the director of genetics. He was so obsessed with the importance of heredity in human behavior that he even coined the term *thalassophilia* (Greek for attraction to the sea) and proposed that it was the consequence of a dominant gene that influenced men's propensity to careers as naval captains. Initially, Davenport shunned attempts to instigate legislation affecting reproduction, but ultimately he was responsible for the cruel suggestion in 1911 that mentally retarded women be segregated from society until post-menopausal, by which time, of course, they would not increase society's burden of mental retardation. By the start of World War II, however, thirty states had laws for compulsory sterilization of the mentally retarded. In 1933, the Eugenics Sterilization Law was passed in Germany, thus setting the stage for the perversion of human genetics that contributed in a major way to the Holocaust.

An illustrative problem from modern human behavioral genetics

To see how behavioral genetics research has the potential to create scientific and social controversy today, let us consider a question that also is the title of an editorial in *Scientific American* (1994): "Is

Homosexuality Biologically Influenced?" The presentation that follows illustrates some of the methods used in behavioral genetics research and the difficulties with interpreting some of the results.

In the same issue of *Scientific American*, LeVay and Hamer (1994) presented evidence for a biological influence on male homosexuality, which is estimated to occur in between 1 to 5 percent of males (and in about the same proportion of females). Two approaches to the problem were taken; first, a search for physical differences between male and female brains and, second, family studies.

Regarding the physical evidence, there are experimental data from rats indicating a dimorphism (a physical difference) in the hypothalamus. In males, the hypothalamus is larger than in females. In addition, there is a group of cells anterior to the hypothalamus that is bigger in males; this is an area that has been shown to be sensitive to androgens, the hormones that promote male sexual differentiation (and prevent female differentiation). The human data, which may indicate a slightly smaller androgen-sensitive region in gay males, are only suggestive and obviously difficult to come by. Even if physical differences were found between the brains of human males and females, and even if those of homosexual males were more like females, many questions would remain, including the time of origin of the differences (for example, early embryo versus adult) and whether the differences were secondary to extraneous causes such as AIDS (many of

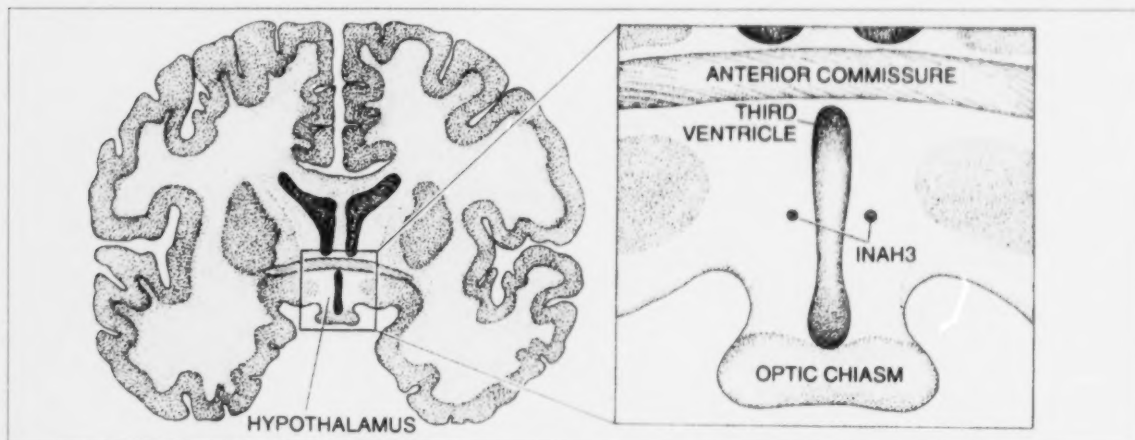


Figure T.7 In Simon LeVay's study, the hypothalamus of the human brain was examined for differences that may relate to sexual orientation. The INAH3 cluster of cells on either side of the third ventricle was found to be larger in heterosexual men than in homosexual men and heterosexual women.

the male brains analyzed came from men who died of AIDS-related diseases). Moreover, even if the differences are real, they may not indicate anything about the causation of homosexuality.

As we will address in the classroom activities for the students (although not in the context of homosexuality), family and twin studies are important investigative tools for the behavioral geneticist. If there is a genetic component to homosexuality, then we would predict a higher incidence of homosexuality among close relatives than would be expected among the general population. Until recently, the stigmatization from admitting to homosexuality was so intense that many denied their sexual orientation, even to themselves. The stigma has lessened somewhat and there have been many reports indicating an increased familial incidence of homosexuality. The importance of comparing identical (monozygotic, MZ) twins with fraternal (dizygotic, DZ) twins and nontwin siblings is self-evident: MZ twins share their entire genomes; DZ twins share an average of 50 percent of their genomes, as do nontwin siblings. If a trait were entirely determined by a gene or genes, theoretically there ought to be 100 percent concordance (or correlation) for that trait in MZ twins. In other words, if one MZ twin were affected, the co-twin always would be affected as well (see Box I). The concordance for DZ twins would be much less and about the same as for nontwin siblings. The ideal study model is twins of both types raised in the same home compared with twins raised apart after separation at birth or shortly thereafter. The latter model is difficult and expensive, and such twins were not available for the above research. Here is a summary of the family study results:

- for homosexual men
 - 57% of MZ twins were concordant for homosexuality
 - 24% of DZ twins were concordant
 - 13% of nontwin brothers also were homosexual
- for homosexual women
 - 50% of MZ twins were concordant for homosexuality
 - 16% of DZ twins were concordant
 - 13% of nontwin sisters also were homosexual

Additional observations included the statistic that family clustering (two or more homosexual siblings) was most obvious for same sex relatives and less so for male-female pairs. It was clear from the research

that the frequency of affected twins and nontwin siblings was much lower than would be suggested by single-gene inheritance. The researchers also noticed that most of the homosexual relatives were on the maternal side of the family, which suggested a possible sex-linked form of heredity, either due to a gene on the X chromosome or an autosomal dominant gene associated with sex influence, perhaps similar to the postulated mechanism for male pattern baldness. After conducting an association study (which the students model) using DNA markers, the researchers localized a specific region of the X chromosome that was more common in homosexual males than would be expected by chance alone. The investigators were convinced that they had demonstrated a genetic component to homosexuality. It is interesting that a genetic association study failed to find any link between homosexuality and the region of the X chromosome identified by Hamer and his colleagues (Rice 1995). [Note: Hamer replies that this study used DNA mostly from gay men with paternal homosexual uncles, which would not be expected to show the effect since it is postulated to be inherited on the X chromosome.] Failures to replicate the results from behavioral genetic studies are common, a testament to the complexity, difficulty, and lack of consensus that typifies investigations of human behavior.

In an accompanying paper titled "The Biological Evidence Challenged" by William Byne (1994), the author attempts to refute the evidence presented for a biological basis for sexual orientation, especially homosexual orientation. He begins by stating that the salient question is not *whether* biology is involved but *how* it is involved because, ultimately, all psychological phenomena are biological. Another important issue is the definition of sexual orientation: Is it really a dimorphic trait? Are men *programmed* for attraction to women and are women generally programmed for attraction to men? In such a framework, male homosexuals would have female programming and female homosexuals would have male programming. Some investigators say the programming occurs prenatally; others think it occurs after birth in response to social factors and various experiences. In fact, the notion that homosexual men are feminized and female homosexuals masculinized may say more about our culture than about the biology of erotic responsiveness. Some Greek myths held that those with predominantly same-sex desires were the most manly of men and the most womanly of women, and classical culture

BOX I

Correlation

Most of the methods in behavioral genetic research, such as twin studies, make inferences to genetic and environmental effects by using some measure of association between different classes of relatives. Although advanced methods use a statistic known as *covariance*, we will discuss a simpler measure of association called **correlation**. Correlation is a statistic, the value of which indicates the magnitude and direction of association between a pair of measurements (usually two types of relatives such as pairs of identical twins). The value of a correlation can range from -1 to +1. A value of +1 denotes a perfect positive relationship between two sets of measurements. This means that if you know the value of one of the observations, you can predict the value of the second observation, and they go in the same direction. For example, if a school bus happens to pass your house every day precisely when you leave for work, the correlation between the appearance of the bus and your leaving for work is 1.0. With that information, a naive observer could accurately predict that when the bus was still a block from your house you soon would get into your car to leave home. A value of -1 denotes a perfect negative relationship; in this case, you still can predict one value from the other, but they go in opposite directions. Zero denotes that the two observations are unrelated. A value in between -1 and +1 other than 0 indicates that there is a less-than-perfect relationship between the measures. Notice that correlations do not necessarily indicate causation. In our previous example, leaving for work does not *cause* the bus to arrive. You just happen to leave your house at the same time the bus is making its rounds to pick up students.

The scatterplots for risk scores generated in *Activity 3: A Novel Trait*, are graphical representations of the information summarized by correlations. If all of the points fell directly on a diagonal line that increased from left to right, this would indicate the presence of a correlation of +1. If all of the points fell upon a diagonal line that decreased from left to right, this would indicate presence of a correlation of -1. The extent to which individual points deviate from a straight line is an indication of how less-than-perfect the relationship is. In the case of zero correlation, the individual points are scattered at random and there is no "best" way to draw a line through the points.

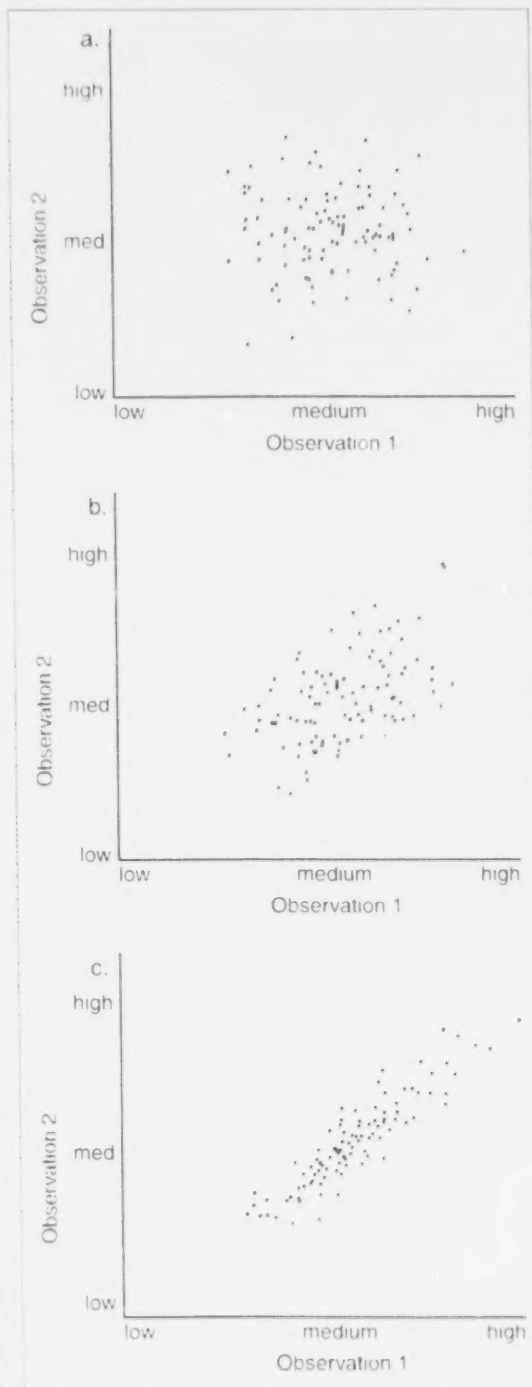


Figure T.8 Panel a. no correlation; Panel b. low correlation of 0.2; Panel c. high correlation of 0.8.

celebrated the homosexual exploits of archetypally masculine heroes such as Zeus, Hercules, and Julius Caesar. The author argues in effect that sexual orientation is likely more complex than a dimorphic trait.

The possible anatomical differences in brain structure between the sexes have been difficult to corroborate among studies in humans, with the exception of the observation that on the average males have larger brains with greater numbers of neurons than females. Even if that turns out to be *correlated* with sexual orientation, that fact by itself does not prove that it has anything to do with *causation*. Byne goes on to refer to considerable data on the hormonal and social contributions to sexual orientation, including the research on individuals born with ambiguous genitalia who have been reared in the sex assigned to their genitalia rather than that of their sex chromosome constitution. As adults, most have become normally oriented in the sex of assignment. (On the other hand, sex reassignment when development has proceeded normally, however, is often not effective. Until recently, when a male infant has had his penis amputated due to accident, the standard approach was to surgically create a vagina and raise the child as female. Long-term studies of such individuals have rarely shown them to adjust easily to their female status.)

Byne's comments on the family studies were as follows. One might expect that DZ twins would have had about the same proportion of concordance as nontwin siblings. The lower figure for the latter is not dealt with by LeVay and Hamer, but it could be influenced by such environmental factors as shared intrauterine environment and the fact that DZ twins are the same age, nontwin siblings obviously are not. Thus, there will be, for example, sharing of friends and classroom experiences among DZ twins that does not occur among nontwin siblings. These are environmental, not genetic, influences. Furthermore, there have been studies showing that the incidence of homosexuality in *adopted* brothers of homosexuals (11 percent) was much higher than the rate of homosexuality in the general population. Obviously, that observation challenges a simple genetic hypothesis and strongly suggests a significant environmental component to sexual orientation. Also, the concordance between MZ twins for homosexuality is relatively low and certainly allows for a significant environmental component to sexual orientation. As mentioned earlier, it would have

been useful to corroborate either the importance of the role of environment or the role of genetics through studies of twins raised apart, but this was not practical.

Byne concludes by emphasizing just how little we know about the origins of sexual orientation and how much further researchers must go before they understand the factors, both biological and experiential, that contribute to this highly complex trait. To quote his conclusion:

Perhaps more important, we should also be asking ourselves why we as a society are so emotionally invested in this research. Will it—or should it—make any difference in the way we perceive ourselves and others or how we live our lives and allow others to live theirs? Perhaps the answers to the most salient questions in this debate lie not within the biology of human brains but rather in the cultures those brains have created.

This module will deal with the appropriateness of behavioral genetic research and the ethical, legal, and social implications of the results that emerge from such research.

The impact of genetics on society

Although interest in and studies of human genetics date back to the 19th century, humans have been difficult subjects for research. (Actually, genetic studies date back to biblical days if we include the observation of sex linkage for hemophilia, which the ancient Hebrews discovered as a result of the ritual of circumcision of males. They waived the ritual for brothers and other maternally related male relatives of bleeders.) The reasons are fairly obvious and include long generation times; small family sizes; the ethics of obtaining specimens, such as blood, from children too young to provide informed consent; and limited access to internal organs and tissues.

With the emergence of molecular genetics in the modern era, progress in human genetics was still impeded, not so much by problems with obtaining specimens for DNA study but by the lack, until recently, of a genetic map allowing human genes to be located along the chromosomes on which they reside. Among the major achievements in molecular genetics was the discovery of DNA polymorphisms,



Figure T.9 James Watson, codiscoverer of the structure of DNA, was the Human Genome Project's first director.

variations in the DNA sequences among individuals that could be used as markers of unique chromosomal locations. With that discovery, it became conceivable that the entire human genome could be mapped and eventually sequenced.

The boon to the research community has turned out to be enormous. Scanning segments of the human genome looking for mutations and matching newly discovered human gene sequences with known sequences already described by other investigators has been moving forward rapidly as a result of publicly available data from many laboratories. The first congressionally mandated money for what is known as the Human Genome Project (HGP) became available in 1987, a time when many molecular geneticists were still arguing about whether the whole project was worth the billions of dollars, yen, and other currencies that it would require.

As project director of the Human Genome Project beginning in October 1988, Dr. James Watson (codiscoverer of the structure of DNA) ensured that 3 percent of the National Institutes of Health-funded component (about 3 percent of \$200 million annually) should support research and discussion on the ethical, legal, and social implications (ELSI) of the new knowledge. This was the largest sum ever provided by the U.S. government for the study of the ethical implications of biological research. Watson felt that his position as director of the HGP, while still director of the Cold Spring Harbor Laboratory, the former site of the Eugenics Record Office, might raise concerns about the eugenic implications if genes involved in influencing behaviors were identified. Immediate worries about the misuse of genetic information generated by the HGP by insurance agencies, governments, and prospective employers led to monies being provided by ELSI programs for public forums and educational and research projects to discuss these issues right from the start. This module, and the three previous BSCS genome modules, are products of ELSI funding. We present a more detailed discussion of ELSI issues in another section of this background material, but the following words from Dr. Watson are pertinent:

From their beginnings, our ELSI programs had to reflect primarily the needs of individuals at risk of the oft-tragic consequences of genetic disabilities. Only long-term harm would result in the perception of genetics as an honest science if ELSI-type decisions were perceived to be dominated either by the scientists who provided the genetic knowledge or by the government bodies that funded such research.

[Keynote address, Congress
of Molecular Medicine, May 1997]

What Is Behavior?

Broadly defined, behavior comprises the reactions and interactions of an organism to its environment and with other organisms. In a general sense, anything an organism does is behavior. When we refer to human behavior, we also consider what people think and feel as well as what they do. Thus, behavioral geneticists consider personality traits and intelligence as behaviors, which may seem odd to students who equate behavior with the mating activities of sticklebacks and prairie chickens.

It is important to understand the meaning of the words we use to describe behavior, and the word behavior itself, because we are using these words in a scientific context, and the meanings of these words in a scientific context are often different from their meanings in ordinary usage. For example, when people use the word *depression* in casual conversation, it may mean a feeling that everyone experiences from time to time as a part of normal life. In a medical context, however, it refers to a specific set of symptoms with defined severity and duration. Many of the words that we use here to define a behavior may sound familiar, but we often use these words to mean something more specific than the common usage. Therefore, when we are using common words to say something specific, we will provide a definition.

Why should we be interested in the biology of behavior?

To survive, individuals must express behavior. At a very basic level, people must find food successfully; eat; obtain shelter; communicate and interact with

others; and, at a more sophisticated level, do all of the things that are required to build and maintain a complex society. Many of the behaviors that are needed to maintain the structure of our society are taught and learned; others seem to occur naturally.

Some behaviors are triggered by basic biological needs such as hunger. It is a reasonable assumption that our ancestral environment would have selected for behaviors that addressed such needs. Thus, it is not surprising that most people exhibit predictable behaviors in response to hunger. Other behaviors are more complex skills that are needed to function socially. Some behaviors at the extremes of the range can be damaging to the individual and to society and are seen as pathological. Those extremes of behavior, such as severe mental retardation (which might be seen as an extreme condition of low intelligence), can result from the failure of a physical process to take place in its expected way. Normal behaviors directly and indirectly affect an individual's health and how long he or she will survive. Even chronic diseases, such as heart disease, cancer, and diabetes, are influenced by behavioral lifestyle habits. Thus, it is impossible to consider any aspect of human existence without considering behavior.

What factors contribute to individual differences in behavior?

Everyone is different. Any trait we examine, whether physical or behavioral, exhibits variability. The fact that this variability exists is important for allowing us to adapt to a wide variety of conditions. For example, some individuals have a metabolic rate that

allows them to eat all they want and not gain weight. In our society, these individuals have little difficulty in maintaining a healthy weight (and as a result, they do not suffer medical consequences from obesity), and they are often the envy of their friends because they are thin. In time of famine, however, such individuals would be more vulnerable to malnutrition than their friends whose metabolisms allow them to store their food calories more efficiently.

Analogously, high levels of risk-taking behavior can damage an individual's chance of survival if the behavior exposes him or her to increased danger. Sometimes, however, taking a risk is necessary for eventual survival. Consider an isolated community of one hundred individuals who are exposed to a great threat such as being out in a field surrounded by lions and tigers. Ten risk-taking individuals decide to leave the community under cover of darkness to establish a new outpost. We could imagine that by the next morning, the remaining ninety individuals could have been attacked and eaten while the ten risk-takers are safe in a cave. Or the risk-takers might have been attacked and eaten immediately upon leaving the community, satisfying the appetite of the beasts who then wander off. Under either of those scenarios, variation in risk-taking behavior has ensured the survival of the community in one form or another. Thus, it was in the interest of the community or population to sustain a high level of variation for the trait: no single behavior could have guaranteed the survival of the community under both circumstances. As with all organisms possessing advantageous traits (or adaptations), the processes of evolution provide a mechanism for selecting the variants in each generation that are best equipped to deal with the challenges of the environment.

Behavior is influenced by genes and environment.

Every person must exhibit certain behaviors that are critical for life, and the species must maintain a pool of individuals that contains behaviors consistent with the production of offspring. Those behaviors include the ability to procure meals successfully in a competitive environment; eating; avoidance of obvious mortal danger; and, for at least a subset of the population, finding a mate and reproducing. It is beneficial to the species for those behaviors to occur naturally. Even a newborn infant knows without being taught how to suckle to obtain milk. As devel-

opment progresses, feeding behavior becomes more complex and is subjected to a range of individual experiences and environmental influences. Thus, even though all of us experience the urge to eat, each of us maintains substantial control over the process of choosing to eat a particular meal. Clearly biology and environment (including experience) both play roles in this critical behavior.

Biology's role in behavior is obvious because all behavior is controlled by the brain and the nervous system. Genes choreograph the development of the brain through transcription and translation of DNA into proteins. Through those processes, genes affect the molecular structure of the brain at every level, including brain anatomy, neurotransmitter levels and receptors, and the processes that control the development of interconnections among neurons. Environment also plays a role by modifying or disrupting genetically encoded actions. Variation in the genes that control brain development may result in variation of behavior.

It is not necessary to consider anything as complex as brain anatomy to see that genes may influence complex behavior. Consider a simple, metabolic process. Variation in the gene that codes for aldehyde dehydrogenase, an enzyme that functions in metabolizing alcohol, can result in an inactive enzyme. When individuals who have only the mutated form of this gene drink alcohol, they cannot break down a toxic alcohol metabolite. As a result, every time they drink alcohol, they get sick. As a further consequence of this mutation, they are less likely to drink alcohol than people without this genetic variant. In other words, a gene influences their drinking behavior.

Although genes are responsible for the biological substrates of behavior, behavior also is influenced by experience and other aspects of the environment. When we talk about the environment, we mean a person's culture, experience, and interactions with family and friends, as well as anything else that is nongenetic, including prenatal exposure to toxins, a brick falling on the person's head, and an infection with a pathogenic agent that has some effect on the central nervous system. Using drinking habits as an example, some individuals never even try alcohol because of religious beliefs or cultural influences. Because exposure to alcohol is necessary for behaviors related to alcohol consumption to be expressed, these people never express an

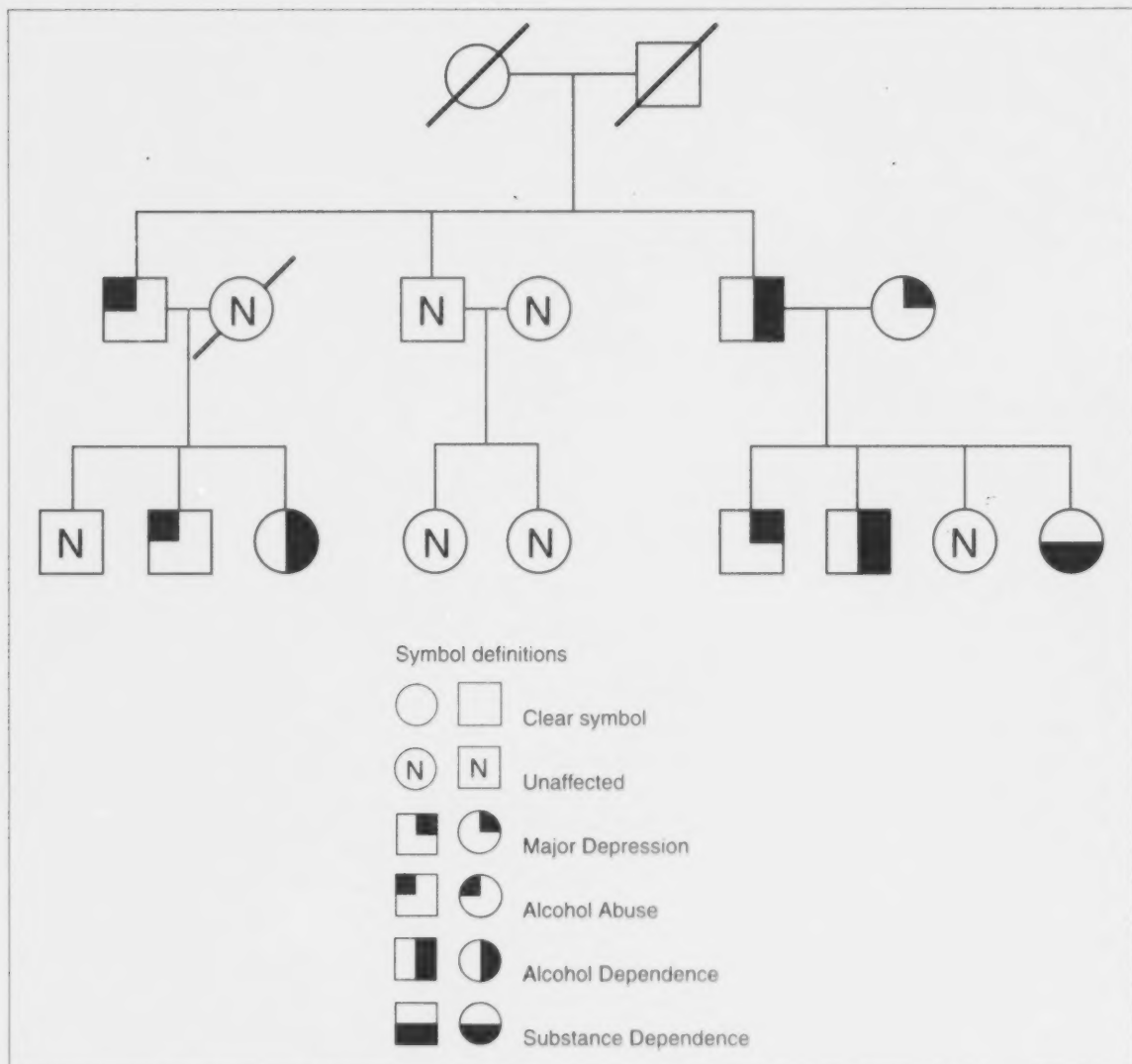


Figure T.10 Pedigree of a family affected by alcoholism.

entire set of behaviors. Some cultures provide greater opportunity for exposure than other cultures. For example, regular consumption of alcohol with meals is the norm in some cultures or families but is discouraged in others.

At a different level of environmental influence, alcohol can act as a prenatal environmental toxin when consumed by pregnant women during a specific period of fetal development. One possible outcome is reduced cognitive capacity (intelligence) of the child. Another example of an environmental toxin is lead exposure, which is a commonly recognized

problem for inhabitants of older buildings in which lead-based paint has been used or lead is used in the plumbing. At certain stages of development, lead exposure also can lead to reduced cognitive capacity. In both of those examples, toxins prevent the brain from developing normally, which results in effects on behavior.

Although we have discussed how genetics and environment influence behavior and, to some extent, form the substrates of behavior, it is rare for a particular outcome in a particular situation to be wholly specified by these factors. That is, the influences of

the environment and genetics do not supplant volition, and behavior is not *determined* by experiences or genes.

Behavior can be influenced by development.

You can never step into the same stream twice. The brain is not a static organ throughout the lifespan because the effects of genetic and environmental influences on the brain are not constant. They vary depending on the age of the individual. Development is sequential in nature: what an organism is today depends on what it was yesterday and is a substrate for what it will be tomorrow. Certain genes are active only at certain developmental stages, act differently depending on the stage, or are otherwise affected by context. Thus, developmentally influenced behaviors depend on historical events, the timing of which may result in differing behavioral outcomes even when the genetic background is constant. Because their context is historical, genes influence developmental and behavioral possibilities but do not determine them entirely. That is why identical twins really are not identical.

How do we measure behavior?

Some behaviors can be measured simply by observation or some objective measure. For example, alcohol consumption can be measured in mouse studies by monitoring the amount of alcohol the animal chooses to drink given a choice between an alcohol solution and water. Activity levels can be quantified in mice by determining how often a mouse crosses a grid line in its cage, or in humans by a mechanical strap-on device that measures how often a person moves. Violence can be measured by how often a person has been arrested for assault. Reading disability is often assessed using standardized tests.

Some behaviors can be observed directly but must be interpreted by the observer. For example, a knowledgeable observer can detect differences between modes of interpersonal interaction of a person with schizophrenia and a person without schizophrenia. Many psychiatric diagnoses are made through direct interview. Research interviews exist in standardized format to ensure that certain questions are asked in a certain order. These direct interviews are frequently used for research diagnoses. Use of such instruments allows behavioral researchers to improve the validity and reliability of diagnoses.

Other behavior measurements rely on self-report and, therefore, must be filtered through the individual's experience. These would include either reports of thoughts and feelings or the person's reporting of his or her actions such as the amount of alcohol consumed over a period of time. Self-report instruments often are used to provide numerical measurements of personality characteristics. In general, the more interpretation that is necessary, either by the subject or the observer, the more likely it is that imprecision can be introduced in the measurement of behavior. In psychiatry, it is simply a fact that some diagnoses can be made with higher degrees of precision and objectivity than others.

Although the measurement of behavior presents challenges, the desire to reduce uncertainty due to subjectivity in measurement has motivated behavioral scientists to pay particular attention to issues of measurement and reliability. In addition, it is important to recognize that nonbehavioral measurements also present challenges. Nonbehavioral traits that at first glance might appear to be unaffected by measurement issues also suffer special problems of their own that contribute to uncertainty in measurement. For example, blood sugar levels vary throughout the day and in response to recent food intake. So a single measurement may not provide an accurate assessment of glucose metabolism. Blood pressure levels are influenced by stress and other aspects of the measurement environment. By contrast, certain behavioral and personality characteristics, such as extroversion (outgoing personality), are relatively stable. Thus, behavior is not unique; issues involving imprecision in measurement occur regardless of what kind of trait is being measured.

- Waiting in line, do you often
 - a. chat with others
 - b. stick to business
- Do you tend to
 - a. say right out what's on your mind
 - b. keep your ears open
- Do you consider yourself
 - a. a good conversationalist
 - b. a good listener

Figure T.11 Excerpt from the Keirsey Temperament Sorter II, © David Keirsey.

Methods and Assumptions of Research in Behavioral Genetics

The goals of research in behavioral genetics are to answer questions about the existence and nature of genetic and environmental influences on behavior. Questions arise at a variety of levels of inquiry, and there are different methods that have been developed to answer different types of questions.

The basic genetic questions are:

1. Does a behavioral trait run in families?
2. If it does, can genes help explain family resemblance and individual difference?
3. If so, what is the nature of the genetic influence (in other words, is it inherited in a Mendelian pattern or is it something more complex)?
4. Where in the genome are the genes located?
5. What proteins (gene products) do the genes encode?
6. How does each gene product function?

With these questions in mind, there are two primary types of methods: those based on the principles of genetic epidemiology and those that employ the technology of molecular genetics. In genetic epidemiology (the study of the clustering of specific traits in families and populations), the goal is to provide designs that permit quantification of genetic and environmental effects. In molecular genetics, the goals are to establish the biochemical basis of genetic effects. Animal studies are an important approach because they allow the direct manipulation of genetic backgrounds as a means to studying behaviors.

Methods using principles of genetic epidemiology

To quantify genetic and environmental effects, methods in genetic epidemiology are designed to subdivide variability among members of a specified population into genetic and environmental components. Frequently, the environmental influences are broken down further into those that are shared by family members and those that are unique to the individual. Heritability (see Box II) is a commonly used term that describes the proportion of phenotypic variation among individuals in a specific population that can be attributed to genetic effects. The reason many behavioral geneticists focus on the genetic effects is that the chromosome theory of inheritance and the central dogma of molecular biology provide a theoretical context for investigating and testing genetic hypotheses. No equivalent, comprehensive, theoretical framework exists for studying environmental effects.

Family studies. An obvious place to look for genetic effects is within families. Family studies are useful because families are easy to find, and most family studies can provide information about genetic influences on a trait, mode of inheritance (for single-gene traits), and sometimes number of genes involved (for polygenic, or multiple-gene, traits). The obvious problem with relying on resemblance among family members is that they share environmental influences as well as genes. For example, if we merely determine which traits run in families and assume that all traits that run in families are genetic, we will falsely

BOX II

Heritability

Many of the genetic studies, such as twin studies, that are discussed in this module are designed to provide an estimate of the relative importance of genetic and environmental effects. *Heritability*, often denoted as h^2 (which is technically the doubled correlation coefficient for the first-degree relatives discussed below), is an estimate of the relative importance of genetic influences on a trait. (Analogously, one could consider a statistic that indicates the relative importance of the environment, denoted e^2 , that is equal to $1 - h^2$.) The value given to a heritability estimate is the proportion of phenotypic variation in a population that is attributed to genetic influences. This value is relevant only to the *particular population being studied at a particular time and under a particular set of environmental circumstances*. A heritability estimate that is obtained from an isolated population in Iceland is not necessarily applicable to any other population.

It is critical to recognize that heritability is a characteristic of a *population*, not of an *individual*. As an example, consider a population of three individuals whose height you measure. One individual experiences a nutritional deficiency during development that makes him shorter than his full potential for growth. The other two individuals do not experience such a deficiency and reach their full growth potential. For the first individual, the environment is an important factor, whereas the height of the second and third individuals is influenced almost completely by genetic influences. Although heritability for this *population* might be estimated to be 70 percent overall, the relative importance of genes and environment varies dramatically at the level of the individuals within the population. This is an extremely important, and little known, limitation of heritability estimates. What it means is that in no case can scientists use a heritability measure to say that an *individual's* intelligence potential, for example, is limited because genes contribute 50 percent to that trait. For that *individual*, the learning environment may be significantly more important than for the average population.

conclude that traits such as religious affiliation, wealth, and preference for cold cereal have a genetic basis. We can conclude from family resemblance that there *may* be genetic influences on a trait, but we need more specialized approaches to separate genetic influences from shared environmental influences.

Twin studies. Identical twins provide an experiment of nature where both members of a twin pair are entirely alike for all of their genes on average. Fraternal twins, in contrast, are genetically like nontwin siblings in that they share only half of their genes. Both kinds of twins share environmental influences to a similar degree (but greater than might be expected for nontwin siblings). Because identical twins and fraternal twins differ only in the amount of DNA that they share, greater similarity for a particular trait in identical twins than in fraternal twins is evidence for a genetic contribution to that trait. If identical and fraternal twins are similar for a particular trait, this is evidence for a shared environmental contribution to the trait.

The ability to separate genetic and shared environmental influences using twins is a powerful advantage

of using twins. A further advantage is that both members of a twin pair are the same age. Since many behaviors are affected by age or developmental stage, this is an important advantage over family studies, where age can differ by an entire generation. A disadvantage of relying on twins is that they are more difficult to find than families. A critical implicit assumption is that identical twins and fraternal twins share environments to the same extent, which may be an overly simplistic assumption. There are other more complicated issues that arise in the context of twin studies that are beyond the scope of discussion in this module but that must be considered by scientists when interpreting results.

Adoption studies. Both twins and other family members share environmental influences to some extent. The study of children who have been adopted at an early age provides a unique opportunity to separate genetic effects cleanly from shared environmental effects. Any systematically observed similarity for a given trait between biological parents and adopted-away children must reflect genetic, rather than environmental, effects. In contrast, any systematically observed similarity between adoptive

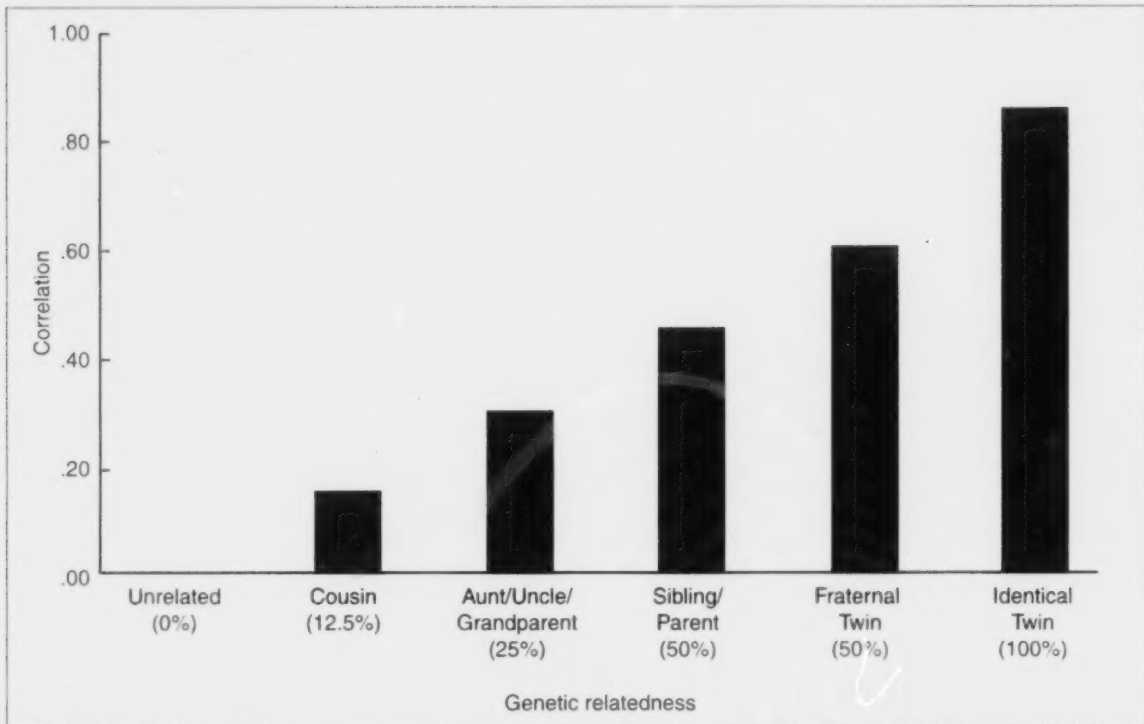


Figure T.12 The rationale behind family and twin studies: If genes are important in influencing a behavioral trait (and assuming that environmental influences are more or less equal), then the correlation between relatives should increase as genetic relatedness increases.

parents and children they have adopted must reflect shared environmental effects. The clean distinction between shared effects that are genetic in origin and shared effects that are environmental in origin makes the adoption study design appealing and powerful (although there are possible confounding factors, such as prenatal environmental influences). On the other hand, adoption studies are extremely difficult to conduct because there are very few children who are adopted in contemporary society, and there are serious issues of confidentiality that make it difficult to link adopted children to their biological parents. Furthermore, adopting parents tend to be older, wealthier, and healthier than the corresponding biological parents, who frequently are very young and usually are in difficult life circumstances. These sampling issues raise questions about the general applicability of conclusions drawn from studies of this sort. Historically, adoption studies have been very important in psychiatric genetics, particularly for establishing a genetic basis for schizophrenia at a time when wholly environmental hypotheses were heavily favored.

Methods using molecular genetic technology

The methods described in the previous section cannot be used to actually locate genes. Molecular genetic technology describes a set of methods involving the direct study of DNA. Such methods are used in all modern gene localization and identification studies. At this point, it will be useful to review some basic terms we will need to use. Alleles are different forms of the same gene. If there are multiple possible alleles for a gene, the gene is said to be **polymorphic** (many forms), and the variation itself is called a **polymorphism**. Most gene localization studies make use of polymorphic **genetic markers**, which are pieces of DNA (usually with no known coding function) of known chromosomal and regional location and multiple allelic forms. These markers have been identified throughout the genome on every chromosome as part of the Human Genome Project. Markers can be measured with relative ease in individuals and provide a series of signposts used to identify the location of particular genes in a consistent way.

The use of markers for gene localization is conceptually simple. If related individuals share identical marker alleles, then they can be inferred to share DNA sequences near those markers. If enough related individuals share both a trait (such as a particular disease) and a particular marker allele, a gene influencing the trait may be inferred to exist close to the marker location.

Linkage analysis. Linkage analysis is used to "map" (or locate) genes by studying their transmission in families with respect to other genes (or genetic markers) of known location. If trait and marker are transmitted together within families or shared by siblings, the gene is inferred to be close to the marker. The gene and the marker are then said to be

linked. If there is no relationship between relatives sharing a marker allele and relatives sharing a trait, it is assumed that there is no gene for the trait in the vicinity of the marker.

Linkage analysis has been used classically for Mendelian traits. For complex traits, types of linkage analyses known collectively as **nonparametric methods** (in that basic genetic parameters, such as mode of transmission, do not have to be specified for the analysis to be valid) are used. The basic principle is the same: if relatives—commonly, sibling pairs—share both trait and marker alleles, the gene must be close to the marker location. When this method is applied to traits that vary continuously, such as height or propensity to take risks, in contrast

BOX III

Quantitative Trait Locus Analysis Using Sibling Pairs

A particular method for identifying specific genes that influence quantitative traits (quantitative trait loci, or QTLs) that is receiving wide application is the use of sibling pairs. This approach capitalizes on the fact that there will be variability in the degree of genetic similarity at any individual chromosomal region between a pair of siblings. Even though siblings share half of their genetic material, this is an average over all genes. At specific genes or marker locations, some siblings will share exactly all of their genetic material (two alleles); others will share exactly half of their genetic material (one allele); yet others will share none of their genetic material (0 or neither allele). This is illustrated in

Figure T.13.

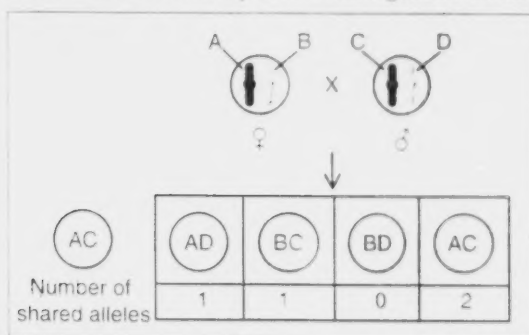


Figure T.13 QTL analysis using sibling pairs.

Consider a gene that has four alleles: A, B, C, and D. The mother has alleles A and B and the father has alleles C and D at the gene. Each child of these parents can receive either allele A or B from the mother and either allele C or D from the father. This means that there are four possible combinations or genotypes that a child can inherit from the parents: A and C, A and D, B and C, or B and D. Which genotype one child inherits is independent of the genotypes that any other children in the family inherit. Comparison of the genotypes in the figure illustrates that one child (for example, with

genotype A and C) can share either two alleles with a sibling (of genotype A and C); one allele (with siblings of either genotype A and D or B and C); or no alleles (if the sibling is genotype B and D).

If pairs of siblings who share two alleles are more alike for a quantitative trait than pairs of siblings who share one allele, who in turn are more alike than those who share zero alleles, we infer that this gene influences the quantitative trait. If we do not observe a relationship between the degree of genetic similarity at the gene and degree of similarity for the quantitative trait, we conclude that this gene does not have an influence on the trait. Although the details rapidly become very complex, markers instead of actual genes are usually used for this approach. When markers throughout the genome are used, this provides a general solution to identifying all genes that influence traits without requiring prior knowledge either about mode of inheritance or physiology.

BOX IV

Candidate Genes

Candidate gene studies usually are based on hypotheses relating specific genes to specific traits. For example, depression and certain anxiety disorders often are treated by medications that act on the serotonin transporter protein. This protein is important for communication between neurons that secrete the neurotransmitter serotonin. Many other lines of evidence also consistently suggest that serotonin plays a role in generating anxiety and depression-related behaviors. The gene coding for the serotonin transporter protein, therefore, was considered a candidate gene for influencing those behaviors.

Researchers test candidate gene hypotheses using linkage, association, and mutational analysis designs. Genes coding for proteins involved in communication between neurons have generated great interest as potential candidate genes for behavioral traits. Some of these classes of proteins are the enzymes that help make the neurotransmitters and the receptor molecules that let neurons determine when they are being signaled. For example, a gene for a dopamine receptor is a candidate gene for influencing novelty-seeking behavior. This association is described in the section titled *Some interesting results*.

to traits that are all-or-none, such as a presence or absence of a disease, it is known as **quantitative trait locus** (QTL) mapping (see Box III). If a gene that affects such a trait is identified, then it is known as a QTL for that trait. For quantitative traits, it is frequently expected that multiple QTLs will have an influence.

Association studies. In many cases, scientists can formulate a reasonable hypothesis about whether known genes might influence a behavioral trait. If a known gene is thought to influence a trait, it is referred to as a **candidate gene** (see Box IV). Researchers then can test the hypothesis that the gene affects the trait by conducting an association study. In an association study, a comparison is made between observations of particular alleles of the candidate gene in populations of individuals with or without the trait. If a particular allele is observed more often in the group with the trait than in the group without the trait, one possible explanation is that the allele plays a role in influencing the trait. This is the method modeled in the fourth activity, *Finding the Genes That Influence Novelty-Seeking Behavior in Humans*. Often, there are, however, alternative explanations for genetic associations that have nothing to do with the gene influencing the trait. For example, the candidate gene may simply be linked to another gene that actually is responsible for influencing the trait. It is the responsibility of scientists conducting studies of this sort to consider carefully all possible alternative explanations, and only when alternatives are eliminated to make a claim that a gene and a trait are associated.

Mutational analysis and DNA sequencing. When a gene has been mapped to a region of the chromosome by linkage analysis, we know approximately *where* it is, but we do not yet know exactly *what* it is. This is critical information both for deducing the steps in the development of the trait and for eventually being able to identify with greater specificity environmental contributors to the trait. Gene identification is a complex and time-consuming task; it often involves a process called positional cloning, discussion of which is beyond the scope of this module. Eventually, though, specific mutations are identified, either through direct DNA sequencing, or through a set of shortcuts to sequencing known as mutational analysis.

Animal studies

Human studies in behavioral genetics rely primarily on observational data over which we have no experimental control. It is not possible or ethical to manipulate experimentally who marries whom. Animal studies provide an important alternative for studying certain kinds of behavior because the researcher can set up carefully selected patterns of mating under tightly controlled environmental conditions. (For a caveat on environmental control, see "Breaking news" in the section *Some interesting results*.) Results derived from the behavioral studies of nonhuman animals may help us understand how genetics can affect human behaviors. This is because evolutionary theory links us through relatively close phylogenetic relationships to certain nonhuman animals such as mice. Thus, if genetic effects are important in the behavior of nonhuman animals, it is not

unreasonable to expect that some genes may influence some human behaviors. Humans, of course, have a tremendously greater capacity for analyzing and controlling their behaviors than do nonhuman animals.

For these reasons, historically many studies in behavioral genetics have been conducted using non-human species. Behaviorists have used the fruit fly *Drosophila* extensively to study the genetics of simple behaviors, such as geotaxis (attraction to gravity) and phototaxis (attraction to light). Hundreds of mutations that affect behavior have been identified in the fruit fly. A closer biological relative to humans is the mouse, which is a mammal. The mouse and human genomes have been shown to overlap substantially, with many DNA segments containing genes in the same order in the two species (synteny) and with very similar DNA sequence and identical function (homology).

Selection studies provide a powerful tool for detecting genetic influences on behavior. In selection studies, quantitative traits are measured in animals of mixed genetic background, which leads to a continuous distribution of phenotypes. Those animals that exhibit high and low extremes of the trait are selected as parents for the next generation. This process is repeated over a number of generations. If the trait is genetic, there will be divergence over time in the value of the trait in the offspring of parents selected for high and low values. Figure T.14 shows the results of a classic selection study of maze-running behavior in mice.

Studies of inbred strains and derived generations are a second strong approach for detecting genetic variation in quantitative traits. Inbred strains are strains in which siblings have been mated over many generations, resulting in strains in which all animals are virtually genetically identical and all genes are homozygous. Differences between strains are attributed to genetic influences, whereas variability within strains is attributed to environmental influence. A great deal of information about genetic and environmental influence is also obtained from derived generations such as the F_2 , which is the cross between two inbred strains resulting in offspring all of which are heterozygous at all genes, with one allele from one parental strain and the other allele from the second parental strain. All individuals in the F_2 generation are genetically identical heterozygotes.

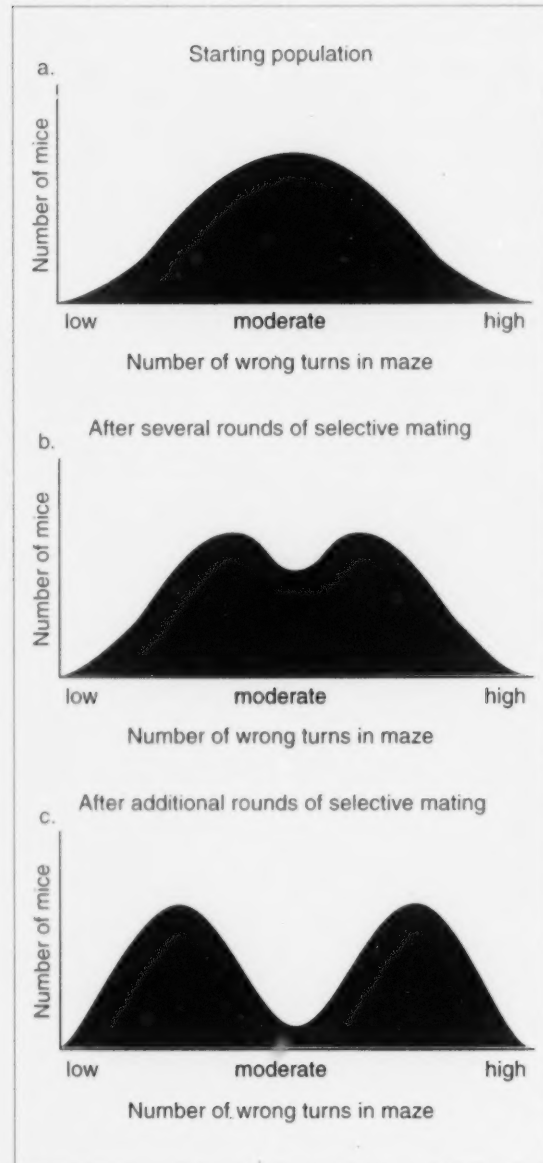


Figure T.14 Animal selection study. *a.* If scientists test many mice for their ability to run a maze successfully, they find a wide range of behaviors. This graph shows the typical distribution for a trait exhibiting continuous variation. *b. and c.* If scientists choose maze-bright mice from this group and mate them with other maze-bright mice, they eventually end up with a population of maze-bright mice with only a narrow range of behavior. Likewise, a population of uniformly maze-dull mice can be bred if maze-dull mice are mated with other maze-dull mice from the starting population. This experiment illustrates that complex behaviors have genetic components.

Subsequent generations, such as the F_2 , which results from mating individuals from the F_1 generation, will have a mix of genotypes from both parental strains, with (on average) $\frac{1}{4}$ being homozygotes identical to

one parental strain, $\frac{1}{4}$ being homozygotes identical to the second parental strain, and $\frac{1}{2}$ being heterozygotes similar to F_1 individuals. There are predictable patterns of mean differences as a function of geno-

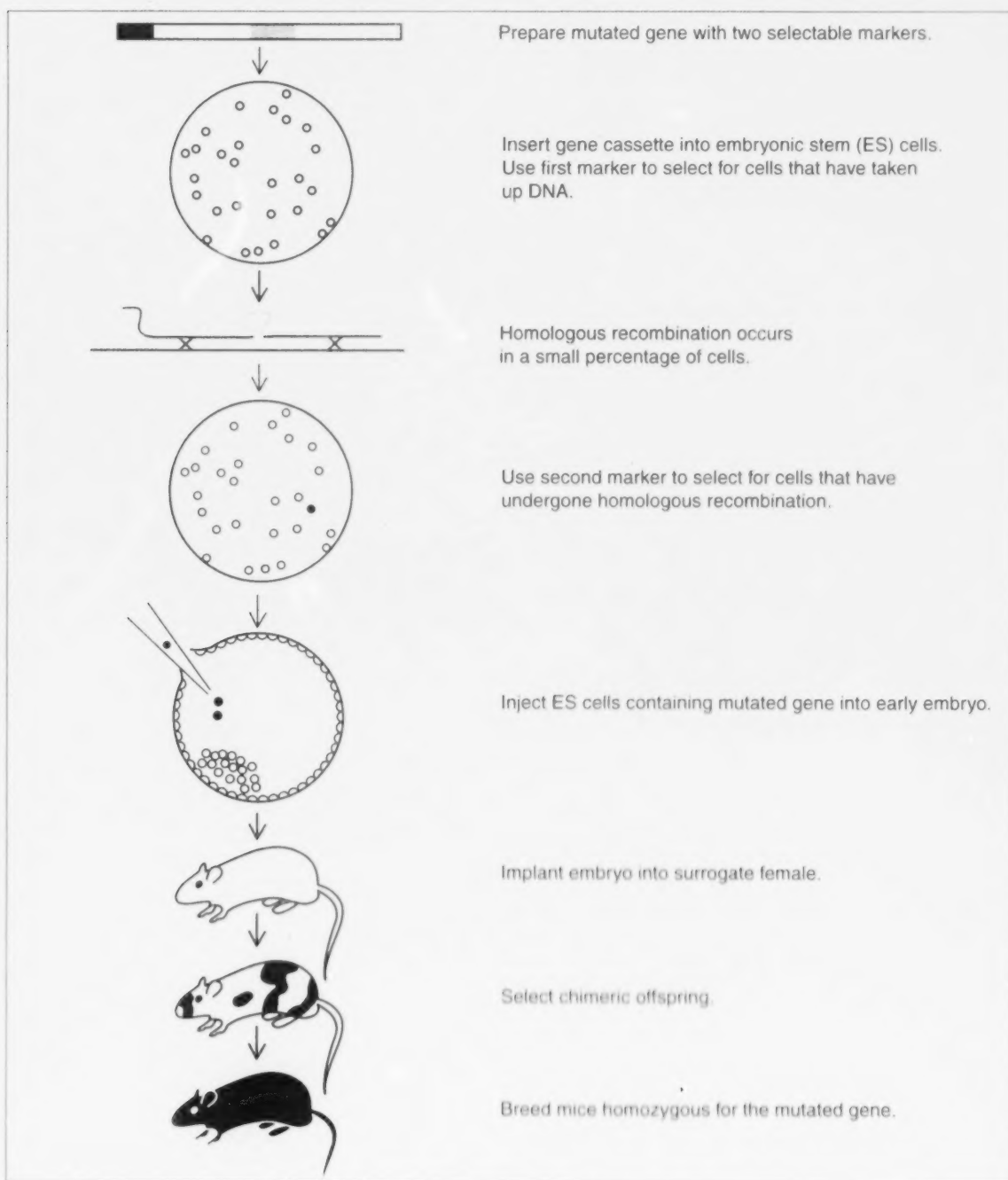


Figure T.15 Procedure for creating a mouse with a mutated (or knocked-out) gene.

type that are used to infer the presence of genetic influences.

Transgenic and knockout mice result from new technologies that permit an investigator to insert a foreign gene or delete a specifically targeted gene, respectively. Differences in the behavior of the transgenic or knockout mice compared to mice without the insertion or deletion imply an influence by that specific gene on the behavioral trait. Those technologies also allow researchers to determine aspects of the function of a particular gene that could not otherwise be measured. For example, by knocking out the gene that codes for a nerve-cell receptor for the neurotransmitter serotonin, scientists increased the aggressiveness of male mice. Similar studies are allowing profound increases in the ability to understand the activity of specific genes.

Some interesting results

For every behavioral trait that scientists have investigated using epidemiological or molecular techniques, some level of genetic influence has been found. Although that may seem startling, it should not be. After all, every inherited physical trait has a genetic component, and behaviors are just as reliable as heritable indicators of species as any physical trait. Although the behaviors of many nonhuman animals are among the most visible examples of the heritability of behaviors, here we will discuss briefly some of the more relevant and interesting results from human studies.

Novelty seeking. Fortuitously, novelty seeking (the focus of the third and fourth activities), the tendency to seek out and enjoy novel, and sometimes risky, experiences is one of the best studied personality traits. Through twin studies, behavioral geneticists found that this trait, defined somewhat differently in different studies, was better correlated between identical than fraternal twins. These findings suggested that genes influence the trait. Subsequent studies at the molecular level confirmed an association between novelty-seeking behavior and a gene for a particular neuroreceptor, the dopamine D4 receptor (*D4DR*). This association is interesting because neuroreceptors are known to be involved in regulating mood. Indeed, they often are the targets of mood-altering drugs such as Prozac, which affects serotonin transmission. Thus, it seems plausible that the implicated gene might exert a physiologically relevant effect.



Figure T.16 Sky surfing is an example of novelty-seeking behavior.

In two separate studies using different populations and different but related novelty-seeking surveys, scientists identified a polymorphism in *D4DR* that correlates with novelty-seeking behavior. *D4DR* alleles that contain six to eight repeats of a 48 base-pair (bp) sequence correlate with higher than average novelty-seeking scores. *D4DR* alleles that contain two to five repeats correlate with lower than average scores. There is a significant overlap in the scores, indicating that the effect of the *D4DR* locus on novelty seeking is small (about 4 percent), but the effect was specific. No similar correlations were identified between *D4DR* and reward dependence, harm avoidance, or persistence.

Schizophrenia. Schizophrenia is a chronic and disabling mental illness involving onset in early adulthood; deterioration in level of function; and psychotic symptoms (inability to distinguish between one's thoughts and reality), such as auditory and visual hallucinations and paranoia. Until the 1960s, many psychiatrists accepted the idea that schizophrenia was caused principally by family environmental factors, for example, the interaction between the preschizophrenic child and his or her mother. A series of landmark adoption studies carried out in the 1960s demonstrated that the risk for schizophrenia of adopted-away offspring of schizophrenic parents was higher than the risk to adopted-away offspring of nonschizophrenic parents. Those

results were confirmed by subsequent studies. In addition, twin studies consistently have shown increased concordance (sharing of diagnosis) for identical compared to fraternal twins. Family studies also have shown increased rates of schizophrenia in siblings, parents, and children of schizophrenics. Recent linkage studies have provided fairly consistent evidence that a gene predisposing to schizophrenia resides on chromosome 6 and less consistent but still reasonably good evidence for genes in other chromosomal locations.

Dyslexia. Genes also have been mapped for specific reading disability (dyslexia). Reading disability has been shown to run in families, where siblings and parents of reading-disabled children perform worse on reading tests than siblings and parents of children who are not reading disabled. Twin studies have shown higher concordance rates in identical twins compared to fraternal twins, which suggests that reading disability is moderately genetic in origin. Recent research has provided evidence that there is a gene involved in reading disability on chromosome 6 and another on chromosome 15. Although only the approximate locations of the genes have been identified, and not the genes themselves or the mechanism through which they influence reading disability, it is interesting that the two genes appear to influence different component processes of reading skill. Phonological awareness is related to a region on chromosome 6 and single-word decoding is related to a region on chromosome 15.

Bipolar affective disorder. Bipolar affective disorder, also known as manic-depressive illness, is characterized by both episodes of depression (sad mood, alterations in sleep and appetite, feelings of hopelessness and worthlessness) and mania (euphoric or irritable mood, increased activity, racing thoughts, decreased sleep). Bipolar affective disorder is different from major depression, which has a slow onset but generally lasts for months and is more common than bipolar disorders (about 3 percent of the general population versus 1 percent for bipolar affective disorder). (Interestingly, each generation since World War II has had a higher incidence of major depression, a trend that supports significant environmental influence.) Bipolar disorder involves rapid mood swings, and the manic periods can be as short as days or as long as months. Family and twin studies have consistently indicated a strong genetic component. Recent linkage studies have identified

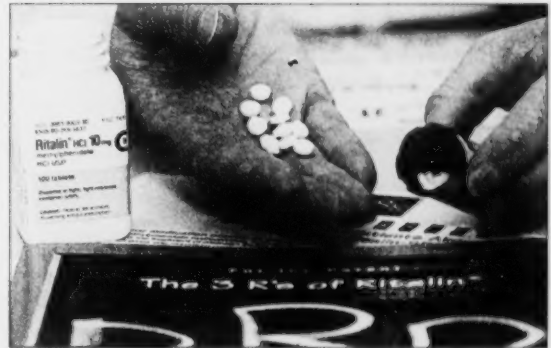


Figure T.17 Ritalin is a behavior modification drug administered to children diagnosed with ADHD.

at least two potential locations for genes that increase susceptibility for bipolar affective disorder, but at present no specific genes have been identified.

Attention deficit hyperactivity disorder (ADHD). ADHD is characterized by problems with maintaining attention and by impulsivity and hyperactivity. Although this is a disorder with strict diagnostic criteria, it is sometimes diagnosed casually and inappropriately in children, especially boys, whose behavior is really within the normal range. A complicating factor for diagnosis is that even children without true ADHD may improve behaviorally when given common ADHD treatments such as Ritalin, so improvement does not aid in diagnosis. With these cautions under consideration, the heritability estimates for ADHD as derived from twin studies are quite high, generally over 50 percent. There is tentative evidence suggesting that the dopamine transporter protein gene may be involved in predisposition to ADHD.

Alcohol and drug dependence. Both alcohol and drug abuse have distinct and overlapping genetic predisposing factors. This is not surprising given that most drugs of addiction and alcohol act on the same reward pathway in the brain, the nucleus accumbens and ventral tegmentum. There is suggestive evidence for the genetic association of several specific genes and alcohol dependence. There is some evidence that the genetic factors leading to alcohol dependence differ between men and women.

General cognitive ability (intelligence). Intelligence, the general capacity to learn and solve problems, has been shown in numerous studies to be heritable,

with about half of the variability attributable to genetic factors. (Note that this is not the same as saying that half of intelligence is attributable to genetic factors.) The observation that there is a significant genetic contribution to intelligence is not seriously disputed because of the amount of work done in this area, an enormous body which has been subject to extremely careful scrutiny. No specific genes contributing to normal variation have been indisputably identified, but many genes contributing to very low intelligence (such as mental retardation) are known.

Breaking news. In a recent study, scientists tested the reproducibility of behavioral genetics experiments conducted in different laboratories. Three groups of researchers located in Portland, Oregon; Edmonton, Alberta, Canada; and Albany, New York, applied the same set of tests to the same strains of mice under nearly identical conditions but obtained different results. The three groups tried to control for as many genetic and environmental variables as possible. They used the same numbers of mice, fed them the same food, used the same light/dark cycle, and even performed their tests on the same day at the same time.

In one standard test that measures anxiety, called the "elevated plus-maze," mice are placed into an apparatus that resembles a horizontal plus sign suspended about one meter above the floor. Two arms of the apparatus have transparent side walls, while the other two arms are open. Scientists measure how much time mice spend in each of the two types of environments. Mice that prefer the safety of the walled arms are termed "anxious," while mice that spend more time on the open arms are considered "less inhibited." When the results were compared from the three laboratories, scientists found that mice in the Edmonton lab were uniformly less anxious, regardless of the strain tested.



Figure T.18 Mouse in an "elevated plus-maze" that is used to measure anxiety.

When knockout mice lacking a receptor for the neurotransmitter serotonin were tested in the elevated plus-maze, once again the location of the laboratory made a difference. Knockout mice were more active than the control mice in Portland, less active in Albany, and no different in Edmonton. The Portland lab had previously reported that the knockout mice would drink more alcohol than the control mice. This study seemed to confirm a role for serotonin in alcohol addiction. When the test was repeated across the three laboratories, however, none of the labs reproduced the effect. It may be that the mice were detecting environmental differences imperceptible to the investigators, such as smells in the laboratories.

This study serves as a cautionary tale regarding the significance of findings in behavioral genetics: subtle differences in environment can have large effects on the behavior being measured. If such large environmental effects are seen in mouse studies, then certainly they will be important for studies of human behavior.

Ethical, Legal, and Social Implications of Behavioral Genetics

The Human Genome Project (HGP) is a large, internationally coordinated effort to map and sequence the human genome. This \$3 billion project involves the collaborative efforts of the federal government and private sector in the United States as well as the governments and scientists of other countries. The U.S. federal government has pledged at least 3 percent of its annual HGP budget to support research and discussions about the ethical, legal, and social implications of findings from genetics research. Members of a variety of scientific agencies, including the Department of Energy, the National Institutes of Health, and other organizations, coordinate the scientific efforts of the HGP.

The National Institutes of Health and the Department of Energy—which is involved because of the effects of radiation on the genome—have independent initiatives to address the ethical, legal, and social issues related to mapping and sequencing the human genome. These activities are known under the acronym, ELSI. The major issues related to ELSI in this module concern the nature of scientific explanations and predictions, including their limits, and the relationship between explanations of human behavior that include a genetic component and explanations that presume our behaviors are independent from genetic influence and solely the domain of free choice.

Explanation and prediction in behavioral genetics

In this module, we distinguish among several ways of knowing or understanding the world. One may

know the world through music and art, metaphysics, science, and other ways. Science as a way of knowing restricts our investigations to the natural world, observable phenomena, and testable hypotheses, but it acknowledges the other ways of knowing. Science as a way of knowing involves two basic tools: explanation and prediction. In the history of science, scientists constructed explanations of present events by referring to other events or to concepts. Over time, explanation by reference to concepts was found inadequate and explanation by reference to events has become the scientific norm. Given that science is an organized pursuit of knowledge pertaining to natural phenomena, science explains these phenomena in terms of other phenomena that precede that being explained.

In particular, science provides explanations of phenomena in terms of their causes. There are two senses of causality. The first accounts for the regular association of events by using statistical methods that reliably distinguish associations due to chance from those not due to chance. The second accounts for regular association by identifying causal mechanisms or processes that result in the associated phenomena. Causal mechanisms are stable, regular, recognizable patterns of events that occur in a particular, measurable order. In biology, mechanistic causes are usually explained by reference to the activity of life-forms and the products of this activity, for example, the production of proteins according to the instructions in DNA.

Adequacy of explanations. The lay and trade press is full of erroneous explanations that do not meet

the standards of good conceptual science. Scientists assess the reliability of an explanation based on its adequacy. Adequacy depends on both conceptual and functional considerations. Conceptually, an explanation is adequate when it is stated as clearly as possible, with well-defined (ideally, quantitative) terms, at the appropriate level of simplicity (as a rule, simpler explanations are more adequate), and when it accounts for most (ideally, all) of the observed regularity and is consistent with existing scientific knowledge. Hypothesis formation involves the development of explanations that meet those conceptual criteria. Hypotheses that do not meet those criteria are not ready for testing. The classroom activities provide an opportunity for students to describe observed variation in traits (height and novelty-seeking behavior) and to explain clearly the complex role of genes and environment in producing those complex traits.

Functionally, an explanation is adequate when it accounts for the observed regularity of associated phenomena. Adequacy is tested two ways: by accepted statistical methods and by laboratory experiments (for example, animal and molecular genetic experiments); clinical experiments (for example, psychiatric disorders); and natural experiments. Natural experimental methods used in behavioral genetics involve twin, adoptee, and family studies.

Adequacy by statistical analysis. Statistical methods are important for behavioral genetics because family studies, twin studies, and adoptee studies are population-based studies, and statistics are a tool for the mathematical analysis of differences between populations. Explaining the variation of traits in a clearly defined population requires population-based analytic methods, and, properly used, statistics is a powerful analytic method. Statistical methods require large sets of data, especially when you are trying to detect small differences and to deter-

mine whether the regular association is not owed to chance. (The smaller the differences you want to measure, as a rule, the larger the sample size required.) In addition, statistical methods involve judgment calls about what level of probability must be established for events to be described as not associated by chance. Students should appreciate that these judgments are not written in stone and that different statistical measures have their own controversies. Indeed, all experimental methodologies have limitations.

In particular, statistical explanations are limited by how much we can generalize from the population studied to other populations. In behavioral genetics, it is almost always the case that results cannot be generalized beyond the specific population studied (for example, Caucasian, homosexual, male Americans over the age of 18). You should be on the alert in the classroom for students who stretch generalizations drawn from one population to another. Use this opportunity to convey the concept that explanations in behavioral genetics are limited. Unwarranted generalizations are a major source of unjustified genetic discrimination and stigmatization (see *Particular ELSI topics*).

You also should be alert to the attempt by students to apply explanations of population-based data to individuals, which is not valid under any circumstances. The important concept is that the properties of sets are not necessarily the properties of the individual members of those sets. In behavioral genetics, a population-based explanation of genetic variation in behavior does not mean that an individual who displays the behavior necessarily has any specific genes. This has to be established independently, by laboratory testing. Nor does it mean that the presence of a gene or genes will lead to specific behaviors. The inappropriate application of validated population-based explanations is a major source of ethical issues related to the Human Genome Project (see *Particular ELSI topics*).

Adequacy by experimentation. Adequacy is also established by laboratory, clinical, or natural investigations that validate causal mechanisms. In other words, the studies demonstrate that a hypothesized cause produces the observed phenomena. This explanatory model for causation in behavioral genetics requires *in all cases* that events be explained by reference to both genes (usually more than one)

Table T.1 Criteria for Adequacy of a Scientific Explanation

An adequate scientific explanation must:
• be stated clearly using well-defined terms • be stated at an appropriate level of simplicity • account for most (ideally all) observations • be consistent with existing knowledge

and environment and the variable causal role of each. *Any proposed explanation of human behavior that fails to make reference to both nature and nurture is by definition inadequate.* You will find yourself emphasizing this point to your students repeatedly because of the widespread belief in our society that genes are fate and that nature and nurture are somehow opposed to each other as competitor explanations when they are, in scientific reality, essential, complementary components of adequate explanations. Indeed, the current intellectual standard in biology is that the "nature/nurture" controversy is a red herring or nonissue and should be retired, once and for all, from biological discourse.

Prediction. Science as a way of knowing is not just interested in explanation, which is retrospective, but in prediction, which is prospective. Scientists are interested in prediction for a variety of reasons. For example, when prediction is established, the possibility of manipulating natural processes opens up. Modern medicine is based on the use of science prospectively to manipulate natural processes to improve human health and functioning. Behavioral genetics already has made—and will continue to make—major contributions to medicine.

In science, prediction is the ability to describe accurately a precise sequence of regularly associated events before they occur. Predictions are developed as testable hypotheses on the basis of explanations and creative leaps that link previously unlinked scientific information or that discern new areas of investigation. Creativity—often in the form of "thought experiments," which have played a major role in the history of quantum physics—plays a major role in science. This point is worth emphasizing to your students, because, for scientists of the first rank, the creativity of their enterprise is one of their main motivations for the years of effort and sacrifice that their work requires.

The adequacy of predictions depends on how consistent the prospective explanation is with existing validated explanations and with actually observed events—either in nature, the clinical setting, or in the laboratory. The more consistent the prediction is with existing explanations and with observed events, the more adequate it is. Consistency is required for predictions to be established or falsified (more often, falsified). Highly adequate predictions

then are used in the clinical setting to design diagnosis and treatment.

Limitations. The limitations of predictions also must be appreciated. Predictions that are not completely consistent with existing explanations are limited because they may be oversimplified. For example, predictions may not adequately take into account biologic or environmental variability. Predictions that are not consistent with observed phenomena are limited because they are too simple or too complex. These limitations require scientists to reformulate and retest predictions, and, depending on the results, revise explanations. For example, early work on the *BRCA1* mutation estimated a risk of breast and/or ovarian cancer of about 80 percent. More recent and more rigorous population-based analyses have revised this risk estimate downward, to about 50 percent. In other words, the estimate of predictive value of a positive *BRCA1* test became lower as the adequacy of explanation of the individual occurrence of breast and ovarian cancer increased. This finding is crucial in cancer treatment, because women who carry the *BRCA1* mutation use this risk estimate when considering whether to have their breasts and/or ovaries removed as a preventative measure. These are both risky surgical procedures and not guaranteed to eliminate disease risk when performed prophylactically. Therefore, they are more justified at the higher risk estimate than they are at the lower risk estimate, with major implications for how physicians should counsel women who test positive for *BRCA1* in the future.

Science is dynamic. Changes in explanations and predictions are normal events in biological science; the clinical application of science in medicine; and science generally, which is a point worth emphasizing to your students. Indeed, this is a lifelong lesson that they will need on many occasions later in life.

When new, seemingly contradictory results are reported, people often complain that scientists and doctors cannot make up their minds, and so they must not know what they are doing. That is a mistaken way to think about science. Rather, as scientific investigations proceed over time, the adequacy of explanations and predictions is challenged by new findings. The history of science is full of such examples, and so, as a scientist, "changing one's mind" (discarding or reformulating hypotheses or reinterpreting results) about the adequacy and limitations

of explanations and predictions is an essential part of science. A scientist who does not change his or her mind in such circumstances invites other scientists and the public to discount his or her views. The lesson for your students is that citizenship in a society like ours that supports a vast scientific enterprise requires disciplined evaluation of new scientific information and what scientists and physicians say about it. The classroom activities in this module are designed to contribute to the formation of such citizenship responsibilities in your students.

Freedom and responsibility

Ethical, legal, and social issues arise about behavioral genetics largely because the explanations and predictions about human behavior generated by this science compete in the wider culture with other explanations of human behavior. These other explanations appeal in one form or other to the concept of voluntariness: roughly, the concept that human behavior is more often than not the exercise of free will. This concept was developed most powerfully from the end of the 16th to the end of the 18th centuries to justify the sovereignty of individuals over themselves and, thus, the illegitimacy of monarchies. There gradually emerged the concept that individuals are self-governing and that state power is legitimate only when free and responsible indi-

viduals consent to it. This is the fundamental political principle of the legitimacy of the state in democracies. Indeed, this concept was used in the 18th century to justify revolution against monarchs in America and Europe.

Some of the philosophers and theologians who developed this concept were aware of the scientific information of their day and thought that they were developing a concept of individual free will that was consistent with science. In the 19th and 20th centuries, however, philosophers began to treat individual free will as a presumption rather than a provable fact. They did so, in part, because the idea of individual freedom had become so common and accepted in democracies that it was taken for granted.

This presumption of freedom grounds the concepts of moral and legal responsibility for one's actions. You cannot be held accountable for what you ought to have done (moral responsibility) if you were not free to have done otherwise. Similarly, in the law you cannot be found guilty and punished (legal responsibility) for an action if you were not free to have done otherwise.

This presumption of freedom resulted in social policies that set very low evidentiary thresholds for who should be treated as free. That is, you do not face a burden of proof to show that you are free. You are presumed to be free and, therefore, others face a burden of proof to show that you lack freedom. Sometimes this burden is met by providing evidence of reduced ability to make decisions. In other words, the presumption of freedom in matters of moral and legal responsibility is open to evidence that human behavior is more a function of genes and environment than of free choices. Thus, explanations and predictions of human behavior generated by behavioral genetics can and do come into competition with explanations and predictions of human behavior based on the presumption of freedom (see *Biology, human nature, law, and public policy*).

This intellectual and, increasingly, political competition of explanations and predictions is a major source of the ethical, legal, and social issues in behavioral genetics. The general considerations concern the compatibility of scientific and freedom-based explanations of behavior. As behavioral genetics continues to develop, its explanations almost never will be completely adequate and its



Figure T.19 © 1999 Sidney Harris.

predictions almost never will achieve 100 percent accuracy, because science almost never reaches those standards. The lack of complete adequacy and predictive power means that some human behavior cannot be explained causally. This is a necessary function of the limitations of behavioral genetics described earlier. The question arises, to what other explanations can we appeal?

One such explanation, which behavioral genetics recognizes, is chance. There is a controversy in behavioral genetics about whether chance means events that cannot yet be explained or whether chance events simply cannot be incorporated into models of behavioral genetics. On the first account, chance presents a challenge for future research to incorporate chance into a genes-plus-environment-plus-chance model. On the second, chance may be a competitor explanation, which could not be incorporated into models of behavioral genetics.

It is crucial for students to recognize that chance is completely incompatible with freedom and the concepts of moral and legal responsibility, which arise from freedom. Chance events, such as quantum events, simply happen; they are beyond human choice. Because the presumption of freedom requires choice, chance explanations undermine this presumption. No one can be responsible, as an author, for events that simply happen. Thus, chance explanations undermine the presumption of moral and legal responsibility. If some event happens by chance, no one chose it and so no one can be responsible for it. Freedom means that you choose the event to occur and so you are responsible for it. It will be essential to point out to students that they should not interpret chance explanation as making room for freedom because it simply does not do so.

Is the presumption of freedom consistent with explanations of behavioral genetics? As a rule, the answer is "yes." Three main reasons support that answer. First, the best explanations and predictions of human behavior generated by behavioral genetics will always be probabilistic and never deterministic. In principle, probabilistic explanations leave room for choice as an explanation of behavior because probability is not certainty. Second, population-based data are not about individuals, and it is at the level of individuals that the presumptions of freedom of individuals and responsibility operate. To use population-based data to undermine the pre-

sumption of freedom is to ignore the limitations of population-based explanations described earlier. Bad science is a major source of ethical errors, such as stigmatization and genetic discrimination (see *Particular ELSI topics*). Third, at the individual level, the inherently unstable relationships among genes, environment, behavior, social structures, and chance limit the explanatory and predictive power of behavioral genetics. This also leaves room for the presumption of freedom and responsibility.

Behavioral genetics challenges the philosophical, theological, and legal presumption of freedom and responsibility. How much room is left for this presumption has become uncertain. This uncertainty is threatening to many people, perhaps some of your students, because they may think that this uncertainty necessarily will lead us to conclude that all human behavior is determined by genes or by genes and environment. Both conclusions are inconsistent with the nature and limits of behavioral genetics, another example of bad science leading to ethical errors. The goal of the classroom activities is to equip your students to respond to this uncertainty with intellectual rigor and a critical perspective, on both scientific grounds and appeals to freedom. Ethics is a practical, intellectual discipline that your students can apply to achieve this rigor.

Particular ELSI topics

Using these general considerations, we now turn to a discussion of particular ELSI topics.

Freedom and determinism. Since the 18th century and the rise of Baconian science, philosophers and theologians have posed the question: If human thought and action were completely determined by physical or biological forces, what would be the status of freedom? The question for our time would be recast as: If human thought and action were completely determined by our genes, what would be the status of freedom? The answer to both questions is, "freedom would cease to exist." The answer is irrelevant, however, because behavioral genetics teaches that the question is based on bad science. No explanation of behavior that appeals only to genes is adequate. That way of thinking reflects the false dichotomy between nature and nurture. Moreover, even explanations of human behavior that derive from a consideration of both genes and environment will have incomplete predictive power. Thus,

behavioral genetics, when its character and limits as a science capable of predicting human behavior are correctly understood, does not generate the problem of freedom versus determinism.

Stigmatization. Genetic stigmatization makes the same mistakes that all stigmatization does. First, it assumes that the characteristics of a population apply directly to its members, an error previously described. Second, it ignores variability and the individual response to variability in the development of one's capacities. In short, genetic stigmatization is an ethical error based on bad science. Students should be taught that such stigmatization and bigotry are usually the result of ignorance of the nature and limits of science. Once people understand these matters, bigotry begins to fade. Only those who are willfully ignorant and bad-willed continue to be bigots. Thankfully, democracies know how to respond to willful, bad-willed bigotry: they prevent law and public policy from being based on such bigotry and they outlaw unacceptable behavior, such as racial discrimination in hiring, that is based on such bigotry.

Genetic discrimination. The major concerns here are discrimination in health insurance, employment, and education. We will consider each of these separately, because they display ethical variability.

There are two types of health insurance, group and individual. Group insurance covers large populations so that the risk and cost of disease and injury is distributed across many individuals. It is illegal to drop someone from a group plan when that individual gets sick or injured, for whatever reason. The issue for group insurance is exclusion of preexisting

conditions, and it is illegal by federal law for many group insurance policies to count genetic predisposition to disease as a preexisting condition. With the increasing popularity of health maintenance organizations, more and more Americans are covered by group insurance. Thus, at the level of law and public policy, genetic discrimination in group health insurance is increasingly a moot social and policy issue.

That is not the case for individual health insurance. From the insurance company's point of view, writing individual health insurance policies involves more risk because the pool is smaller and healthy people tend not to buy such policies. It is, therefore, economically rational for an insurance company to avoid unnecessary financial risk and to manage assumed risk in an economically responsible fashion (whether or not the insurance company has for-profit status in tax law). Disposition to disease, whether from genetic influences (for example, CF); environmental influences (for example, smoking); or genetic-plus-environmental interactions, is economically rational information for the insurance company to want to acquire, so that it can manage risks in an economically rational way by regulating premiums.

The problem then occurs that people at risk for very expensive diseases may be denied coverage and that, if we mandate coverage of these individuals as a matter of law, premiums will rise on all individual plans. As a consequence, some people who presently have such coverage will no longer be able to afford it. Outlawing genetic discrimination in this case would be ethically justified if there were effective strategies to manage the tradeoffs involved, for example, protecting those already insured. Such

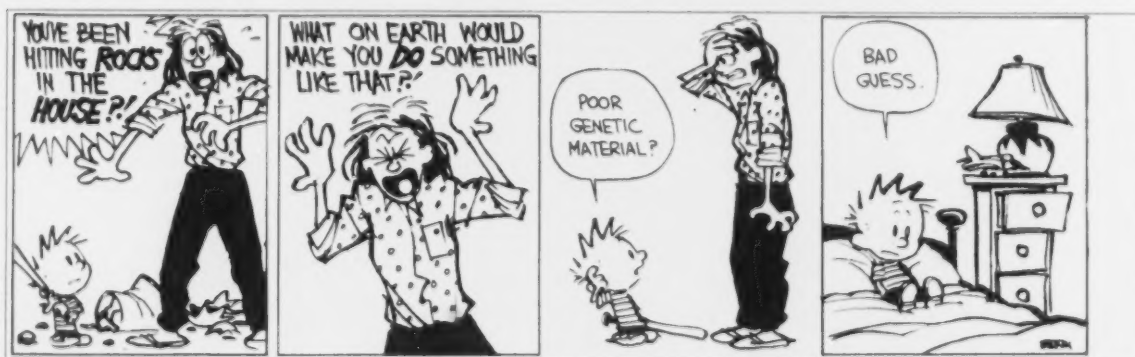


Figure T.20 CALVIN AND HOBBS ©1991 Watterson. Reprinted with permission of UNIVERSAL PRESS SYNDICATE. All rights reserved.

strategies do not now exist. An honest appraisal of the current ethics literature on this topic requires us to report that there is no consensus on this matter.

It is important to note, however, that an insurance company's appeal to economic rationality depends for its ethical justification on the recognition of the nature and limits of genetic science generally, and behavioral genetics, in particular. (The latter will be relevant, for example, for many mental illnesses and disorders, such as depression, which can be expensive to diagnose and treat.) Once again, bad science can lead directly to ethical errors and public policy can be designed to prevent this. For example, policy could mandate that the economic arguments put forth by insurance companies be based on the appropriate use of relevant science.

A recent Supreme Court ruling allowed a company to cap coverage in its health insurance benefits by diagnosis. The case involved AIDS, but the principle

applies to genetic diseases as well. That is, a company could specify caps for particular genetic diseases, such as Huntington disease or schizophrenia, in its health-benefits package.

Genetic discrimination in employment is covered by the Americans with Disabilities Act (ADA). This law prohibits requiring applicants to disclose information about conditions that are or could be perceived as disabilities. Genetic predispositions to disease probably fall under the latter category. Employers are required to make reasonable accommodations for disabled employees, and that would apply to those with genetic predisposition to disease. For example, an employer should make reasonable changes to the workplace to remove deleterious environmental risk factors. The ADA thus renders moot social and policy issues in employment discrimination regarding preexisting conditions.

Genetic discrimination in education will involve troubling uses of scientific information to "track" students inappropriately. The ethical issues here all will involve correcting and preventing ethical errors that result from bad science, such as inappropriate labeling of students as learning disabled, which might occur by applying population-based data erroneously to individuals.

Research with human and animal subjects. Research with human and animal subjects conducted with the support of federal research funds is regulated for its scientific and ethical justification. Research in the private sector undertaken by responsible companies is self-regulated to an unknown degree. These regulations require prior review of research protocols by committees composed of scientists, clinicians, experts in ethics, and representatives of the local community. These are known as Institutional Review Boards (for research involving human subjects research) and Institutional Animal Care and Use Committees.

The essential ethical considerations in animal research are the scientific justification for the research (its demonstrated needs and a sound research design) and the nature, duration, and justification of pain and distress that the animal will experience. Imposing pain and distress must be unavoidable features of the study design and must be justified by the expected value of the predicted results. Because much animal research could not be



Figure T.21 Woman demonstrating for disabled rights.

performed ethically on human beings (for example, deleting an entire gene as scientists do when they create "knockout" mice), animal research plays a major role in behavioral genetics. In addition, because evolutionary biology teaches us that we are, in some genetic respects, similar to nonhuman animal species, results from animal research often can be reliably extrapolated to humans. Finally, preliminary studies of diagnostic and therapeutic interventions need to be tested in animals for their safety and efficacy before being tested in humans. Many innovative interventions are shown to be unacceptably dangerous or ineffective in animal models, thus saving many human subjects from unnecessary exposure to risk of disease, injury, or death.

Research on human subjects also requires that the need for the research and the scientific soundness of the study design be established. The nature of risks must be identified precisely and justified fully. For vulnerable populations, such as children and fetuses, no more than minimal risk may be imposed by the research design. Informed consent is required, except for research in emergency medicine. "No more than minimal risk" is defined in terms of the background risks of the disease. Informed consent by the subject or surrogate is required (unless the subject is incapable of consent, for example, infants or adults with advanced Alzheimer dementia). Emergency research also is exempted from the informed consent requirement. There are special regulations to cover this research.

Medicalization of behavior. One result of the increasing clinical application of behavioral genetics could be the medicalization of behavior. Medicalization is the tendency to view undesirable or uncommon behaviors as pathologies that require treatment. Medicalization may discount or even eliminate explanations of behavior based on freedom and responsibility in favor of explanations based on pathologies, which are not a function of freedom and responsibility.

History teaches that, when medicalization is a function of bigoted ideology and ignores the nature and limits of science, humans will be hurt, as occurred with the medicalization of homosexuality. In that case, patients were declared mentally ill and forcibly treated, often with disastrous outcomes. On the other hand, medicalization has its advantages. Extreme shyness can result in nontrivial mental illness and

seriously impaired social function (for example, hardly ever leaving home and being terrified of job interviews). Behavioral genetics may lead to clinical interventions that both reduce these risks and do not result in unacceptable biopsychosocial side effects. In such a case, medicalization would be a positive phenomenon because it would be based on both good science and careful ethical reflection about the benefits and risks of medicalization. The treatment interventions developed as a result of the medicalization of alcoholism represent another example of the positive outcomes that may arise from recognizing the biological roots of some behaviors.

Eugenics. Eugenics derives from the Greek language and means "well born." Biologically, eugenics is the study or process of improving a species genetically. Many critics and historians of the eugenics movement describe it as a collection of initially well-intentioned efforts to improve health and help those vulnerable to illness that gradually became overzealous. In addition, eugenics represents bad science. It is no surprise, therefore, that the eugenics movement resulted in many ethical errors and contributed to the moral catastrophes of the Holocaust and the Nazi medical war crimes.

Eugenics today is invoked as a "conversation stopper" to condemn various proposed or actual clinical and social policy applications of genetic science. In particular, proposals to enhance human traits, including behavior, are frequently condemned as

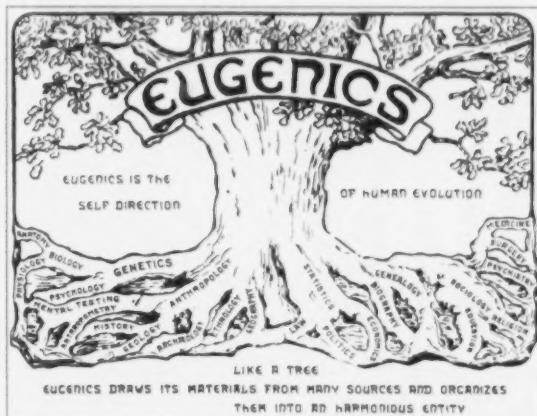


Figure T.22 This description of eugenics from 1921 depicts it as a positive contribution to society. It was based on bad science, however, and was used to justify many discriminatory practices.

eugenics. This condemnation may be premature. First, it is important to recognize that social engineering, such as talented and gifted classes in public schools and the U.S. Olympic Training Center, has been used to enhance human performance for years without anyone objecting to it as unethical because it unnaturally alters human nature. Thus, enhancement, *per se*, cannot be the source of ethical concern. The source of concern arises from the nature of the enhancement: biological, or genetic, manipulation. This brings us to our second point: such manipulations will always occur in the context of environments and will be variable (sometimes highly) in their outcomes. The free and responsible decisions of individuals always will play an important role in human development. Students in your class surely will appreciate that, despite what their parents may think, the students are not simply the average of their parents' genes and environment. To call enhancement eugenics immoral, therefore, is to invoke bad science and to stop conversation prematurely.

An implication here is that germ-line engineering might not be considered eugenics. For example, is the genetic restoration of normal phenylalanine hydroxylase function enhancement or merely the correction of a defect? In discussions of the moral permissibility of germ-line engineering, one will need to take into consideration the positive benefits of manipulating the germ-line, particularly in cases of devastating genetic diseases. Positive benefits, such as the elimination of a fatal or seriously disabling condition, will have to be weighed against harms, such as the burden of genetic intervention. The point here is that one cannot assume that germ-line engineering is—all things considered—eugenic practice and thus morally prohibited.

That conversation needs to consider the kind of human behavior that we most likely will use genetic science to enhance: human disease. Modern medicine is based on the assumption that we should manipulate nature to diagnose and treat disease provided that the cure is not worse than the disease. That is, the morbidity and mortality risks of a disease are the context in which enhancement should be assessed. If such enhancement is reliably predicted to be both effective and less risky than the disease, then enhancement is ethically justified. If that is eugenics, then all of medicine is eugenics and must be stopped, a patently absurd conclusion.

Playing God (forgetting the limits of science).

The phrase *playing God* is used to indicate that somehow or other scientists are tampering with nature in a way that is inappropriate. The phrase implies that some aspects of nature, at least, are sacrosanct and therefore should not be altered or even studied because such knowledge would be dangerous. This charge could be brought against behavioral genetics if it resulted in the manipulation of genes or environment that some people found to be inappropriate.

The concern about behavioral geneticists playing God should be interpreted as the expression of concern that the presumption of freedom and responsibility is given too little scope or eliminated altogether. This worry is almost always unfounded because it assumes that behavioral geneticists can achieve explanations and predications that leave no room for freedom and responsibility, which is almost always false.

Challenges to the criminal justice system. If the explanatory and predictive power of behavioral genetics expands, then the explanatory scope of freedom and responsibility will contract. That calls into question the concept of legal accountability on which the American criminal justice system is built. The issues concern how much legal accountability *should* be called into question.

We know something about this already. Any claim that "my genes made me do it" does not challenge the criminal justice system because bad science never challenges the criminal justice system. Any claim that "my genes and my environment made me do it" must be treated as a scientifically investigatable question. This investigation will be structured by the fact that even the most powerful explanations and predictions of behavioral genetics will be expressed in probabilistic terms, although there may be rare exceptions. The burden will be on those who think there is no room for responsible choice to show that the probability of prediction has reached 100 percent, a very demanding scientific standard. In addition, behavioral genetics today is based on predictions at the population level, not the level of the individual. Caution students that, at the present time, no behavioral geneticist believes that 100 percent genetic prediction for individuals has been satisfied; most would agree that it never will be satisfied.

**Biology, human nature, law,
and public policy**

Recent developments in behavioral genetics, neuroscience, neurology, neurosurgery, and psychiatry are converging on the following view: the structures in the brain and nervous system derive from particular gene products and all voluntary and involuntary behaviors originate or are mediated in these structures. There are two main implications of this provocative claim. The first concerns how we should think of ourselves and the second concerns legal and policy implications of the possibility that some human traits may be less malleable than we thought.

The claim that human behavior is a function of brain structures and that these structures in turn are a function of gene activity presents challenges to other views of human nature. In particular, for centuries in Western thought, philosophers and theologians have held that the mind (for the philosophers) or soul (for the theologians) was a distinct entity, separable or even separate from body (or, as we would now say, brain). Starting in the Renaissance and accelerating during the Enlightenment, this view of mind or soul was challenged by the science of the time and its deterministic concept of causality. There were several responses to this challenge. For the pedagogical purposes of this module, we identify three of the most prominent.

The first was adopted by the 18th-century Scottish philosopher David Hume, who accepted the claim



Figure T.23 Engraving of David Hume (1711-1776).

that psychological phenomena were completely determined by prior physical phenomena as their causes. In other words, Hume accepted the possibility that our choices were controlled by our nervous system. For Hume, however, issues of freedom and responsibility were mainly political, for example, the freedom of the Scottish nation from the English crown. This political concern led Hume to focus on freedom as the absence of external constraints, especially constraints imposed by tyrannical power. Thus, Hume held the view that one might not make one's choices but as long as others did not impose their choices on one, one was free. Law and public policy should aim to secure this freedom from external constraints of tyrannical power.

This remains a viable option, although current science no longer adopts determinism. In Hume's view, scientific information should influence any presumptions that we make about freedom and responsibility. Current science does not support Hume's acceptance of determinism. Instead, the effect of genes plus environment must be understood in probabilistic terms. Current science understands the causality of genes plus environment to allow for the presumption of freedom and responsibility because freedom is part of the environment (that is, it is nongenetic in this view), not a separate or competing source of explanation of human behavior.

A second response to the deterministic concept of causality was to isolate spheres of knowledge or experience from each other, only then to show their interaction. The 18th-century German philosopher Immanuel Kant argued that science never could tell us with certainty what the ultimate structures of the world are, only the causal laws that govern the association of phenomena (what Kant called "appearance," which he distinguished from "things-in-themselves" or the ultimate structures of reality). The effect of this is to remove claims about the mind or soul from the realm of science. Science and morality (along with the law) are distinct spheres of human knowing and experience, governed by different methods and modes of discourse.

At the same time, Kant did not make metaphysical claims about whether there really is a separate entity called the mind or soul. The presumption of freedom and responsibility is thus preserved and



Figure T.24 Portrait of Immanuel Kant (1724–1804).

grounds morality, law, and public policy. Each of us should be treated as if he or she were the author of his or her choices and, therefore, should be held responsible for them. Kant's point is subtle: freedom cannot be proven, is not ruled out by science, and, therefore, must be presumed if we intend to hold people responsible for their behaviors. The meaning of freedom can be influenced properly by scientific information.

This response remains a viable option and is embraced by some behavioral geneticists, although they may be unfamiliar with the Kantian origins of this view. Freedom is not a factor of the environment, but it interacts with genes plus environment and so the two types of explanation of human behavior complement each other.

A third response to the deterministic concept of causality is to hold the claim that mind or soul constitute separable or indeed separate entities that have nothing in common with body or brain. This view finds its historical roots in the dualism of mind and body defended by the 17th-century French philosopher René Descartes. This view has come to be known as Cartesian dualism and its adherents argue that science can make whatever claims it wants about the brain or body, but none of these apply to mind or soul. Mind is really a separate entity, and it is the source of freedom and responsibility, which is not subject to the laws of causality that govern the physical world. Philosophical and reli-



Figure T.25 Engraving of René Descartes (1596–1650).

gious claims about human freedom and responsibility are thus immune from scientific information. Freedom is a function of mind or soul and is an altogether different source for the explanation of human behavior than that offered by behavioral genetics. Freedom-based explanations are not complementary to those of behavioral genetics but in deep competition with them.

We have outlined these three options because they are alive today in public discourse; you can be confident that your students will express some variant of them. These three positions are known, respectively, as Humean materialism, Kantian interactionism, and Cartesian dualism. The final activity asks students to evaluate proposed legislation about beverage alcohol in terms of its assumptions about human nature.

Behavioral genetics, along with other sciences of biology, makes claims that relate to these three views in different ways. Consider the following:

1. Human behavior is simply brain and nervous system physiology. There is no evidence to support the claim for a separately existing entity called mind or soul.
2. As a function of both genes and environment, human behavior exhibits variable malleability. Medical or other environmental interventions (including education and criminal justice) can alter that behavior. Some behaviors will be found to be

Table T.2 Three Prominent Views of Human Nature

View	Description
Humean Materialism	Human nature derives from the physical (brain, nervous system, and body).
Kantian Interactionism	Human nature results from the interaction of the physical (brain, nervous system, and body) and the mind (from which originates freedom and responsibility).
Cartesian Dualism	Human nature derives from the mind, which is separate and distinct from the physical (brain, nervous system, and body).

so strongly influenced by genes that environmental changes should have little effect in changing such behavior. We also should expect some behaviors to be so strongly influenced by environmental factors that genes should have little effect in changing such behavior. In these cases, environmental factors may be more powerful predictors of human behavior than genes.

We consider each claim in turn. In the classroom activities, the first claim is addressed first, because it sets the context and stage for a discussion of the policy issues raised by the second claim.

The first claim concerns who we think we are. We think about ourselves using a highly variable combination of scientific information; philosophical ideas; religious beliefs and traditions; political beliefs and traditions; the ideas of poets, novelists, artists, and musicians; how we were raised; and many other social and cultural factors. Materialists are completely untroubled by the first claim, because it simply states that human behavior is human physiology and experience and nothing more. The interactionist would hold that the truth of the first claim, so long as it is only about phenomena or appearances and not about the ultimate structures of human nature, leaves the presumption of freedom and responsibility undisturbed. The dualist rejects the first claim, either as inadequate or as false. Obviously, the dualist's position is most at odds with behavioral genetics.

The three views respond to the second claim in the following way. The materialist will be quite comfortable with scientifically validated claims that the role of freedom and responsibility as environmental factors may be very small in some cases. Indeed, the materialist expects this to be the case, because of the variable causal strength of genes and environment in explaining human behavior. The interactionist's position is challenged by the second claim, because the greater the explanatory power of behavioral genetics, the less the explanatory power of the presumption of freedom and responsibility. The interactionist may be surprised or even disturbed by this outcome, depending on the importance to freedom and responsibility of the behavior in question. The dualist rejects the second claim because the dualist does not ever accept that scientific explanations of human behavior can affect the presumption of freedom and responsibility. Its scope and importance are never disturbed by the results of scientific investigation.

It is not hard to see at this point why ethical, legal, and social issues regarding the Human Genome Project and the many branches of genetic science are so hard to manage in a pluralistic society such as the United States, especially the social and policy issues. Materialism, interactionism, and dualism have many sincere, well-meaning adherents in American society. These three positions will lead to very different public policies in the final activity. The ethical issues concern how a self-governing society should expect its elected representatives to make public policy in the context of disagreement that is intractable because the underlying intellectual positions of groups of citizens are at times incompatible with each other. This is one of the political problems that the framers of the U.S. Constitution were all too aware of—Madison called them “factions”—and the framers designed our form of government to manage the disagreement of factions. In other words, we have in our political traditions adequate resources to deal with such disagreement.

Public policy

Public policy is a set of guidelines or rules that results from the actions or lack of actions of governmental entities. Governmental entities act by making laws. Laws can be made by legislatures (statutory law); by courts (common law); and by regulatory agencies (regulatory law) at the local, state, and federal levels. All three types of law are pertinent to the

HGP. The law will be concerned for the most part with regulation and funding of the HGP and its applications. With regard to the results from behavioral genetics, the law already applies (for example, the Americans with Disabilities Act). When public policy is a function of law, it is called *de jure* (according to law) public policy. *De jure* public policy may be subject to ongoing debate.

Governmental entities also can make public policy by *not* acting. When governmental entities deliberately or unintentionally do not act, the effect on public policy is to permit individuals and institutions to act in the ways they choose, without the interference of law. Given the complexity of the results of behavioral genetics studies, it is likely that many aspects of the project will not be regulated explicitly by laws. When public policy is not a function of action by governmental entities, it is called *de facto* (actual) public policy. The *de facto* public policy aspects of the HGP will be subject to ongoing debate.

An important condition for making and implementing any public policy is that differing moral positions can produce consensus, even if only a temporary consensus, as the stable basis for public policy that people will accept and follow. The problems with behavioral genetics are such that consensus may be impossible to achieve. One way to read American history is that making public policy in the

face of intractable disagreement is a formula for failure and making things worse. The alternative is no public policy, which, *de facto*, would allow behavioral genetics to continue its work and to disturb such people as dualists. Many might find this offensive. This raises the difficult policy issue of official tolerance of what groups in the population find offensive or even morally unacceptable. This outcome challenges American civility, our historical trait of living with deep moral disagreement without resorting to violence, by committing ourselves to ongoing, mutually respectful, intellectually disciplined conversation. The goal of the last activity is to have your students experience such a conversation in the classroom.

One of the chief roles of public policy is to manage the uncertainty that results when such disparate considerations must be incorporated within the democratic process. For example, policy must decide how much weight should be given to explanations of behavior based on genes plus environment plus chance versus explanations based on the presumption of freedom and responsibility versus protection of the public good. Because the boundary between those three aspects of public policy formation is uncertain and unstable, students may come to the view that no change in public policy is the best short-term (or even long-term) strategy and simply live with the uncertainty.

Glossary

adequacy: (in the context of science) refers to the assessment of an explanation or hypothesis. An adequate explanation is stated as clearly as possible, at the appropriate level of simplicity; accounts for most (ideally, all) of the observed regularity; and is consistent with existing scientific knowledge.

adoption studies: studies that use the separation of biological and social parentage brought about by adoption to assess the relative importance of genetics and environmental influences. Typically, comparisons are made between adoptees' resemblance to their biological parents, who did not raise them to their adoptive parents who did. Other studies compare genetically related siblings and genetically unrelated (adoptive) siblings raised in the same family.

affected: the condition of having a particular trait, usually used in the context of a disadvantageous trait, as for a disease symptom.

allele: one of the alternative forms of a gene at a given locus.

animal selection studies: a tool for detecting genetic influences on behavior. A quantitative trait is measured in animals of mixed genetic background, which produces a continuous distribution of phenotypes. Animals exhibiting high and low extremes for the trait are selected as parents for the next generation. If the trait has a genetic basis, then there will be divergence over time in the value of the trait in offspring selected for high and low values.

association studies: an approach used to test whether a gene influences a trait. Comparisons are made between observations of alleles for a candidate gene in populations of individuals with or without the trait. If a particular allele is observed more often in the group with the trait than in the group without the trait, then that allele may influence the trait.

attention deficit hyperactivity disorder (ADHD): a behavioral disorder that appears to be influenced by genetics. It is characterized by problems with maintaining attention and by impulsivity and hyperactivity.

autosome: a chromosome other than a sex chromosome. Humans have twenty-two pairs of autosomes.

behavior: the reactions and interactions of an organism to its environment and with other organisms.

behavioral genetics: a branch of the life sciences that applies concepts of genetics to the study of behavior. It seeks to understand the role genetics plays in individual differences in behavior.

bipolar affective disorder: (also known as manic-depressive illness) a mental illness influenced by genes. It is characterized by both episodes of depression and mania that can last for days or months at a time.

brain plasticity: a characteristic of neoteny, which describes variations in brain development due to chance that can contribute to differences in behavior.

candidate gene: a gene that is postulated to influence a trait based on one or more lines of evidence such as linkage, association and mutational analysis, or biochemical considerations.

chi-square: a statistical test that evaluates how well a set of observations fit a predicted outcome. The chi-square is often referred to as a "goodness-of-fit" test.

chiasma: (plural is chiasmata) the point of crossing over during prophase I of meiosis in which there is an actual exchange of genetic material between the paired maternal and paternal copies of chromosomes.

coding region: a stretch of DNA sequence (in a gene) that encodes protein.

codominance: the condition in which a pair of alleles for a given locus contributes equally to the phenotype of the heterozygote who bears them.

concordance: the presence of a particular trait in two or more family members, such as twins.

congenital: existing from birth (note that this term does not distinguish whether the condition is inherited, environmental, or both).

continuous variation: a type of phenotypic variation that displays a wide distribution of phenotypes in a population due to the interaction of many genes (polygenic causation) or to genetic and environmental factors (multifactorial causation).

correlation: a statistic that describes the magnitude and direction of association between two measurements or observations. A correlation of 1.0 means that knowledge of one observation reliably predicts the second observation; a correlation of -1.0 means that the two observations are associated in the opposite direction; and a correlation of 0 means that the two observations are unrelated.

credible: (in the context of scientific methods) the condition of being reliable and based on acceptable methods, as in reference to evidence that meets scientific criteria for accuracy and reproducibility.

cytogenetics: a subdiscipline of genetics that combines the study of the cell with the study of genetics,

often focusing on the structure, function, and behavior of chromosomes.

deletion: (in the context of molecular genetics) the absence of one or more nucleotides normally found in a gene, resulting in a mutation.

determinism: a concept from philosophy that maintains that all human thought and action is completely determined by physical and biological forces. A consequence of determinism is that freedom and autonomy cease to exist.

developmental autonomy: (in the context of ethics) having sufficient mental and emotional maturity to be capable of informed consent.

diploid: having two copies of each chromosome; a diploid cell has a chromosome number of $2N$. In humans, the diploid number is 46.

discrete variation: refers to a type of phenotypic variation that displays a small number of distinct phenotypes typically due to the actions of a single or a few genes (for example, Huntington disease; blood groups).

dizygotic (DZ) twins: twins formed from separate fertilized eggs. Fraternal twins share 50 percent of their genes, on average, as with any other sibling.

DOE: the United States Department of Energy.

dominant: the pattern of inheritance in which an allele expresses its phenotypic effect even in heterozygotes and masks that of some other allele at the same locus. A trait expressed by dominant inheritance is called a dominant trait.

dualism: a view of human nature derived from René Descartes' philosophy that maintains that mind and body are separate.

dyslexia: a specific reading disability that is influenced by genetics.

ELSI: Ethical, Legal, and Social Implications, a division of the Human Genome Project.

eugenics: meaning "well born"; an application of human genetics initiated by Francis Galton (1822–1911), Charles Darwin's half-cousin. Eugenics

sought to improve the human species by encouraging those with desirable characteristics to reproduce while at the same time discouraging those deemed "inferior" from having children.

eukaryote: an organism in which cells have a membrane-bound nucleus. Eukaryotes have other subcellular organelles, such as mitochondria or, in the case of plant cells, chloroplasts. Humans are eukaryotes.

gamete: a sexual reproductive cell. Gametes are haploid, having a single (N) complement of genetic material. In humans, the gametes are ova and sperm.

gel electrophoresis: a laboratory separation technique that uses electricity to move molecules through a molecular sieve made out of a gel-like substance, usually either agarose (natural) or polyacrylamide (synthetic). In biology, the technique is used to sort proteins or nucleic acid molecules by their size.

gene: the basic unit of heredity, in terms of function and in the physical sense. A gene is a region of DNA that is transcribed (into RNA) plus the regulatory DNA sequences necessary for transcription. (Not all genes encode protein. For example, in the genes for ribosomal RNA, the transcript is the functional product.)

genome: the entire complement of genetic material. The Human Genome Project defines the human genome as a single haploid set of nuclear chromosomes, plus the mitochondrial genome.

genotype: the genetic makeup of a cell or organism. Genotype can be contrasted with the phenotype (the detectable attributes). Genotype can also refer to the particular allelic makeup for a given gene.

haploid: a cell (or organism) having only one chromosome set (N). See gamete and diploid.

HD: the abbreviation for the human genetic disorder Huntington disease. HD is a disorder of the nervous system, usually with adult onset of symptoms. It often is used as an example of a single-gene disorder. The disorder is fatal.

heritability: the proportion of variation among individuals in a population that can be attributed to genetic effects.

heritable: capable of being transmitted to offspring.

heterozygous: the condition of having two different alleles at a particular locus on a pair of chromosomes (homologs).

HGP: the Human Genome Project; a large, collaborative, scientific research effort funded in the United States by the U.S. Department of Energy (DOE) and the National Institutes of Health (NIH).

homolog: one of a pair of chromosomes that contains equivalent genetic information. In germ-line cells, homologs pair with one another during meiosis. One homolog is derived from the mother and one from the father.

homozygous: the condition of having identical alleles for a particular gene at a given locus in a chromosome pair.

hypothesis: a testable idea or explanation proposed in response to previous knowledge and specific observations.

informatics: the study of information processing. In the field of biology, informatics generally refers to the study of genetic sequence data.

interactionism: a view of human nature derived from Immanuel Kant's philosophy that maintains that there is interaction between the physical (brain, nervous system, and body) and the mind.

karyotype: the entire set of chromosomes of an individual cell made visible by staining and microscopy and arranged by size and chromosome number.

knockout mouse: a mouse that has both copies of a specific gene inactivated using recombinant-DNA technology.

linkage analysis: a laboratory procedure that locates a gene of interest by the presence of identifiable markers located close to the gene.

linked genes: genes located on the same chromosome. Genes that are close together—tightly linked—are less likely to be separated during recombination.

locus: the location of a gene on a chromosome.

marker: (in the context of genetics) an identifiable allele that expresses a known phenotype or a molecular tag (such as a DNA or RNA fragment) to signal the presence of an allele or chromosomal location of interest. DNA or RNA fragments also are used to bind to, and thus identify, a particular genetic sequence in a nucleic acid fragment.

materialism: a view of human nature derived from David Hume's philosophy that maintains that mind and choice are only manifestations of physical phenomena (brain, nervous system, and body).

medicalization: the tendency to view undesirable or uncommon behaviors as pathologies that require treatment.

meiosis: a specialized process of cell division that reduces the chromosome number to the single (haploid) complement (N). Meiosis takes place in germ-line cells. Meiosis produces four haploid daughter cells from one diploid cell, involving one round of DNA replication.

Mendelian genetics: the fundamental concepts of genetic transmission introduced by Mendel and expanded to include knowledge of genetic linkage and sex chromosomes.

mitosis: the process of cell division that ensures that each daughter cell receives an exact copy of the diploid (2N) complement of chromosomes.

monozygotic (MZ) twins: twins formed from a single fertilized egg (identical twins). Identical twins share the same genetic endowment.

mRNA: messenger RNA, the fully processed form of the transcript copied from the DNA sequence of a gene and used to direct protein synthesis.

multifactorial inheritance: inheritance in which the phenotype results from the combined action of genes and the environment.

mutation: a physical change in genetic material, such as base-pair substitution or deletion in DNA. Chromosome breaks or rearrangements involve large-scale mutations. If the mutation occurs in the body (somatic cells), the results affect only the individual bearing those cells; if the mutation is in germ-line cells, the change can be transmitted to offspring.

neoteny: the process in humans (and some other animals) in which stages of growth and development are prolonged well past intrauterine life.

nondisjunction: improper separation of homologs or sister chromatids during meiosis or mitosis. During meiosis, this process can result in a diploid condition for a particular chromosome in one gamete and the absence of that chromosome in another gamete.

nontraditional inheritance: an informal term that refers to new concepts of inheritance that describe processes that were not traditionally understood or taught in Mendelian genetics. For example, imprinting is a process not explained by traditional Mendelian concepts.

PCR: polymerase chain reaction. A laboratory technique that exploits DNA polymerases (enzymes that help replicate DNA) derived from bacteria that live at high temperatures. The technique permits the *in vitro* production of large amounts of a specific DNA sequence from a very small amount of sample DNA. The technique is often used to screen for DNA polymorphisms in populations.

penetrance: the proportion of individuals with a given genotype who express any of the phenotypic features of the trait. Incomplete penetrance refers to the situation in which less than 100 percent of individuals with a given genotype express the associated phenotype.

phenotype: the externally or internally detectable characteristics of an organism, including behaviors, that represent the influences of environmental and genetic information (genotype).

phenylketonuria (PKU): a genetic disorder that results from a deficiency of a liver enzyme, phenylalanine hydroxylase. This lack of enzyme activity results in a toxic buildup of phenylalanine metabolites that lead to tissue damage and mental retardation. Newborns diagnosed with PKU can be placed on a special diet, low in phenylalanine, that can prevent the onset of mental retardation.

polygenic inheritance: inheritance in which the phenotype results from the interaction of several genes, each of which contributes a small effect to the trait in question.

polymorphic: (in relation to DNA) literally, having more than one form, such as different lengths for a restriction fragment or the presence of two or more genetically distinct types in a population.

primer: a short oligonucleotide sequence used to prime enzymatic reactions, such as the polymerase chain reaction (PCR). In the case of PCR, the primer is extended by a polymerase to form a longer DNA strand.

prokaryote: a colonial or single-celled organism whose cells lack a membrane-bound nucleus. A prokaryote has a relatively simple cell structure without organelles such as mitochondria or chloroplasts. Bacteria are prokaryotes.

public policy: a set of guidelines or rules that results from the actions or lack of actions of governmental entities.

quantitative trait locus (QTL): one of multiple genes shown to affect a specific trait.

recessive: a pattern of inheritance in which the phenotypic effects of an allele are masked in heterozygotes when one of certain other alleles is present. A trait expressed by recessive inheritance is called a recessive trait. A recessive trait is expressed only in homozygotes.

restriction endonuclease recognition site: a specific DNA sequence that is recognized and cut (digested) by specific members of a class of bacterial enzymes known as restriction enzymes. This process supplies a naturally occurring immune function for bacteria and is exploited in the laboratory to make possible cloning and other molecular techniques involving specifically sized DNA fragments.

restriction fragment length polymorphisms (RFLPs): the small differences in the length of DNA fragments produced through cutting with restriction enzymes (enzymes that cut DNA at specific sequences). Genetic variation between individuals is reflected in small differences in the length of DNA between the sites recognized by restriction enzymes, thus producing RFLPs. These differences can be exploited to map the location of genes.

ribosome: a structure within cells on which protein synthesis occurs. Ribosomes are composed of ribosomal RNA and proteins.

scatterplot: a graphical representation of correlation data.

schizophrenia: a mental illness having a genetic component. It is characterized by onset in early adulthood, deterioration in level of function, and psychotic symptoms, such as auditory and visual hallucinations and paranoia.

short tandem repeats (STRs): a type of DNA polymorphism that is characterized by varying numbers of repeats of a short DNA sequence (usually 2–4 base pairs). STRs are used as markers to help locate new genes and in forensic DNA testing.

sibling pair analysis: an experimental approach for identifying genes that affect quantitative traits. If pairs of siblings who share two alleles are more alike for a quantitative trait locus (QTL) than pairs of siblings who share one allele, who in turn are more alike than those who share zero alleles, then the QTL is presumed to influence the trait.

somatic cell: a cell that does not produce gametes. In humans, somatic cells are all cells except the germ-line cells in ovaries and testes that will undergo meiosis. A mutation in a somatic cell affects the function of that cell and all body parts derived from it, but it is not passed on to the next generation.

stigmatization: (in the context of genetics) a mark of thinking or behavior that assumes that the characteristics of a set or population apply directly to its members. It ignores variability and the individual response to variability. It is an ethical error based on bad science.

theory: (in the context of science) an explanation of a fundamental principle that has been so thoroughly tested and supported by multiple lines of evidence that it is accepted by the scientific community.

transcription: the process through which an RNA molecule is synthesized by complementary base pairing using DNA as a template. For example, messenger RNA (mRNA) is a product of transcription.

transgenic mouse: a mouse that has one or more genes added to its genome using recombinant-DNA technology.

translation: the process of synthesizing a protein molecule. An RNA message (mRNA) directs the

order of amino acids being bonded together to form a protein. This process takes place on structures known as ribosomes.

trinucleotide repeat: a specific sequence of three nucleotides (subunits of DNA) that is repeated, often in large numbers, in a continuous stretch of DNA in particular genes. The mutant gene for Huntington disease, for instance, contains the trinucleotide repeat CAG repeated many times. *See* short tandem repeats.

twin studies: an experimental approach that seeks to determine the relative contribution of genetic effects to a trait. It involves comparing the phenotypic similarities between identical twins (which share all their genes) with the phenotypic similarities between fraternal twins (which share half their genes, on average).

validity: (in the context of science) the condition of having met scientific criteria, such as being supported by credible evidence, being built on correct premises, and showing sound reasoning.

variable expressivity: the range of phenotypic effects in individuals with a given genotype. (Note that small differences in the genotype may be present but not obvious.)

X-linked trait: a pattern of inheritance in which the allele for the trait in question is present on the X chromosome. Males have only one X chromosome, inherited from the mother. For that reason, X-linked traits cannot be passed from father to son.

zygote: the cell that results from the fusion of a male gamete and a female gamete. A fertilized ovum (egg cell) is a zygote.

References

- Allen, J. E. (1998, June 7.) Novelty-seeking gene expands babies' breadth. [Science Today] *The Denver Post*.
- American Association for the Advancement of Science (AAAS). (1989). *Science for all Americans*. Washington, D.C.: American Association for the Advancement of Science.
- American Association for the Advancement of Science (AAAS). (1993). *Benchmarks for science literacy*. New York: Oxford University Press.
- American Psychiatric Association (APA). (1994). *Diagnostic and statistical manual of mental disorders* (4th ed.). Washington, D.C.: Author.
- American Society of Human Genetics (ASHG) and American College of Medical Genetics (ACMG). (1995). Points to consider: Ethical, legal, and psychological implications of genetic testing in children and adolescents. *American Journal of Human Genetics* 57:1233-1241.
- Associated Press. (1997, June 12). Gene might be girls' edge. [Science] *Colorado Springs, The Gazette Telegraph*.
- Associated Press. (1998, May 11). Primates settle squabbles with a squeeze. *Colorado Springs, The Gazette Telegraph*.
- Associated Press. (1998, June 21). Scientists map genes linked to alcoholism. [Health] *Colorado Springs, The Gazette Telegraph*.
- Benjamin, J. (1996, January). Population and familial association between the D4 dopamine receptor gene and measures of novelty seeking. *Nature Genetics* 12:81-84.
- Benson, E. and B. Rapp. (Eds.). (1998, July). *NCBI News*.
- Biological Sciences Curriculum Study (BSCS). (1999). *Basic genetics: A human approach* (3rd ed.) Dubuque, IA: Kendall/Hunt Publishing Company.
- Bower, B. (1997, July 12). Humanity's imprecision vision. *Science News* 152:26-27.
- Bower, B. (1998, September 5). DNA links reported for schizophrenia. *Science News* 154:151.
- Bradley, A. (1998, December 9). Student-survey dispute spawns more parent rights. *Education Week*.
- Brunner, H. G. et al. (1993). X-linked borderline mental retardation with prominent behavioral disturbance: Phenotype, genetic localization, and evidence for disturbed monoamine metabolism. *American Journal of Human Genetics* 52:1032-1039.
- Byne, W. (1994, May.) The biological evidence challenged. *Scientific American* 270:50-55.
- Campbell, P. (Ed.). (1998, April 30). Therapeutic horizons [Special issue supplement]. *Nature* 392 (6679).
- Casey, D. (1998, January). Cloning: From DNA molecules to Dolly. *Human Genome News* 9:1-2.
- Chorney, M. J. et al. (1998, May 3). A quantitative trait locus associated with cognitive ability in children. *American Psychological Science* 9 (3):159-165.
- Cloninger, C. R., R. Adolfsson, and N. M. Svrakic. (1996, January). Mapping genes for human personality. *Nature Genetics* 12:3-4.
- Collins, F. et al. (1998, July 3). What issues in genetics research most concern 13 experts right now. *The Chronicle of Higher Education* B6.
- Colt, G. H. (1998, April). Were you born that way? *Life* 39-50.

- Crouch, R. A. (1997, July-August). Letting the deaf be deaf. *Hastings Center Report* 27(4):14-21.
- Daniel, C. (1998). Conflicting aims leave ban on human cloning in limbo. <http://washington-post.com/wp-srv/WPlate/1998-07/26/1921-072698-idx.html>.
- Department of Labor, Department of Health and Human Services, Equal Employment Opportunity Commission, and Department of Justice. (1998, January 20). Genetic information and the workplace. Washington, D.C.: The National Human Genome Research Institute.
- Descartes, R. Dualism. <http://serendip.brynmawr.edu/mind/descartes.html>.
- Devlin, B., M. Daniels, and K. Roeder. (1997, July 31). The heritability of IQ. *Nature* 388:468-471.
- Dougherty, M. J. (1997, August 6). Article on genetic defense questioned [Letter to the editor] *Colorado Springs, Gazette Telegraph*.
- Dreger, A. (1998, July 28). When medicine goes too far in the pursuit of normality. <http://www.nytimes.com/library/national/science/072898-sci-essay.html>.
- Eberes, G. and G. Rice. (1995). Preliminary findings presented at the Academy of Sex Research, Provincetown, MA.
- Ebstein, P. et al. (1996, January). Dopamine D4 receptor (D4DR) exon III polymorphism associated with the human personality trait of novelty seeking. *Nature Genetics* 12:78-80.
- Freeman, H. P. (1997, April 9). The meaning of race in science—considerations for cancer research. President's Cancer Panel Meeting. *Cancer* 82(1).
- Gardner, H. (1998, November 5). Do parents count? *The New York Review*.
- Genome project moves up target date. (1998, September 15). *Colorado Springs, The Gazette*, p. A 6.
- Goate, A. and H. J. Edenberg. (1998). The genetics of alcoholism. *Current Opinion in Genetics & Development* 8:282-286. <http://biomednet.com/eleceref/0959437X00800282>.
- Goode, E. (1998, October 20). Old as society, social anxiety is yielding its secrets. <http://www.nytimes.com/library/national/science/102098-sci-health-social.html>.
- Gottesman, I. I., (1997, June 6). Twins: En route to QTLs for cognition. *Science* 276:1522-1523.
- Henig, R. M. (1998, May). Tempting fates. *Discover* 58-64.
- Herbert, W. (1997, April 21). How the nature vs. nurture debate shapes public policy—and our view of ourselves. *U.S. News & World Report* 72-80.
- Hume, D. Materialism. <http://www.utm.edu/research/hume/hume.html>.
- Kant, I. Interactionism. <http://www.friesian.com/kant.htm>.
- Kidd, K. (1993, April 5). Associations of disease with genetic markers: Déjà vu all over again. *American Journal of Medical Genetics (Neuropsychiatric Genetics)* 48:71-73.
- Kiernan, V. (1997, October 3). Cosmetic uses of genetic engineering may soon be a reality. *Chronicle of Higher Education* A17-18.
- Kiernan, V. (1998). Are human behavior and culture products of our biology? *Chronicle of Higher Education* A22.
- Kolata, G. (1998, July 23). In big advance in cloning, biologists create 50 mice. <http://www.nytimes.com/yr/mo/day/news/national/science/sci-cloned-mice.html>.
- LeVay, S. and D. H. Hamer. (1994, May). Evidence for a biological influence in male homosexuality. *Scientific American* 270:44-49.
- Longtin, D. and D. Kraemer. (1998, May 6). Wonders of genetics also carry some risks. *USA Today* 13A.
- Manke, B. et al. (1998, July 3). Genetic contributions to adolescents-extrafamilial social interactions: Teachers, best friends, and peers. *Social Development* 4:3:238-256. <http://blackwell-publishers.co.uk/scripts/webjhs3.idc?scici=0961205X43238256>.
- Mansfield, B. K. (Ed.). (1998, July). *Human Genome News*.
- Maranto, G. (1998, May 26). On the fringes of the bell curve, the evolving quest for normality. *The New York Times*.
- McClearn, G. E. et al. (1997, June 6). Substantial genetic influence on cognitive abilities in twins 80 or more years old. *Science* 276:1560-1563.
- McDonald, K. A. (1998, October 9). Early birds, night owls show gene differences. *The Chronicle of Higher Education* A20.
- McGee, G. (1997, March-April). Parenting in an era of genetics. *Hastings Center Report* 27 (2):16-22.
- Mitchell, A. (1998). Worming out social secrets. *Nature* 395:327.
- Nash, J. M. (1998, April 27). The personality genes. *Time* 60-61.
- National Center for Genome Research (NCGR). (1999, January). *NCGR News* 4(1).
- Nature Genetics*. (1997, August). Cloning Questions. 16(4):317-318.

- New York Times*. (1998, March 11). It's a fact—human pheromones exist. [Health and Science].
- Painter, K. and N. Hellmich. (1998, August 24). Book says parents just play genetic part in personality. *USA Today*, pp. D1, D2.
- Pearlstone, N. (Ed.). (1998, April). *Life*.
- Pfaff, D. W. (1997). Hormones, genes, and behavior. *Proc. Natl. Acad. Sci. USA*. 94:14213–14216.
- Plomin R. and J. C. DeFries. (1998, May). The genetics of cognitive abilities and disabilities. *Scientific American* 62–69.
- Reich, T. et al. (1998, February 26). Genome-wide search for genes affecting the risk for alcohol dependence. *American Journal of Medical Genetics (Neuropsychiatric Genetics)* 81:207–215.
- Riechmann, D. (1998, May 8). Boys admit risky behavior. *The Denver Post* 17A.
- Robertson, J. A. (1998). Human cloning and the challenge of regulation. *The New England Journal of Medicine* 339:(2).
- Rosin, H. (1998). Cloning: Another religious divide. *The Washington Post*. <http://washingtonpost.com/wp-srv/WPlate/1998-07/24/0681-072498-idx.html>.
- Rutter, M. and R. Plomin. (1997). Opportunities for psychiatry from genetic findings. *British Journal of Psychiatry* 171:209–219.
- Saltus, R. (1998, September 30). Scientists discover maternal-instinct gene in mice. *The Denver Post* 11A.
- Shüklenk, U., E. Stein, J. Kerin, and W. Byne. (1997). The ethics of genetic research on sexual orientation. *Hastings Center Report* 27(4):6–13.
- Silver, L. M. (1997, November). Genetics goes to Hollywood. *Nature Genetics* 17:260–261.
- Spitzer, R. L., et al. (1994). *Case book: A learning companion to the diagnostic and statistical manual of mental disorders* (4th ed.). Washington, D.C.: American Psychiatric Press, Inc.
- Travis, J. (1998, May 23). Another human genome project. *Science News* 153:334–5.
- Voll, D. (July, 1998). An American family. *Esquire* 123–128.
- Wade, N. (1998, May 14). Newly found gene may be key to high I.Q. *The New York Times*.
- Wade, N. (1998, August). In the hunt for useful genes, a lot depends on 'Snips.' *The New York Times*. <http://www.nytimes.com/library/national/science/081198sci-snips.html>.
- Wade, N. (1998, September 9). Can social behavior of man be glimpsed in a lowly worm? *The New York Times*.
- Watson, J. D. (1997, May 3). *Genes and Politics*. Keynote address presented at the Congress of Molecular Medicine, Berlin, Germany.
- Weiss, R. (1995, September 20). Gene jewels: Scientist hopes to fashion a fortune from celebrity DNA. *The Washington Post*, P.F.1.
- Weiss, R. (1997). Cosmetic gene therapy's thorny traits. *The Washington Post*. <http://search.washingtonpost.com/wp-srv/national/science/ethical/cosmetic.htm>.
- Weiss, R. (1998). Scientists clone adult lab mice. *The Washington Post*. <http://www.washingtonpost.com/wp-srv/WpPlate/1998-07/23/1331-072398i-dx.htm>.
- Weiss, R. (1998, March 22). Engineering the unborn. <http://search.washingtonpost.com/wp-srv/national/science/ethical/unborn.htm>.
- Wheeler, D. (1997, October 17). Seeing the mind as software written by evolution. The Faculty: Research. *The Chronicle of Higher Education* A16.
- Wickelgren, I. (1998, April 24). Tracking insulin to the mind. *Science* 280:517–519.
- Williams, W. M. (1998, May 15). Democratizing our concept of human intelligence. *The Chronicle of Higher Education* A60.
- Wilson, E. O. (1998, April). The biological basis of morality. *The Atlantic Monthly* 281(4):53–54.
- Wright, R. (1998, August 24). The power of their peers. *Time*.
- Zabludoff, M. (Ed.). (1997, October). Why we do what we do [Special issue]. *Discover* 18(10).
- Zabludoff, M. (Ed.). (1998, May). Racing into the biotech future [Special issue]. *Discover* 19(5).

Classroom Activities: Teacher Pages

Activity 1

Investigating Complex Traits

Overview

In this activity, students become engaged in the biology of human behavior by exploring intelligence. (Although intelligence is not a behavior *per se*, behavioral geneticists refer to human characteristics and qualities, such as intelligence, neuroticism, and happiness, as behaviors.)

The activity begins with a fictitious newspaper article. The inflammatory headline, which implies a single gene determines intelligence, is designed to catch students' attention and initiate a discussion of intelligence. The Analysis Questions will help you introduce some of the module's major concepts and also will serve as a review of basic Mendelian genetics. The concept of codominance is mentioned in the newspaper article. It refers to a type of Mendelian inheritance where each of two alleles for a trait contributes to the corresponding phenotype. In the heterozygous state, where one copy of each allele is present, the resulting phenotype will be a blending of the two different homozygous phenotypes. Students must be familiar with this concept and its expected inheritance pattern to evaluate the hypothesis. The latter point is important because the students will discover that simple inheritance cannot explain intelligence (or complex traits generally). If necessary, review codominance with the students before starting the activity.

Major concepts

- Complex human behaviors are difficult to define and measure.

- Intelligence is not determined by simple codominant inheritance.
- Intelligence shows many phenotypes.
- Intelligence is affected by genetic and environmental factors.

Estimated time

20–30 minutes

Learning outcomes

In this activity, the students will

1. discover that it is difficult to define and measure intelligence;
2. apply the principles of Mendelian genetics to evaluate the hypothesis that the inheritance of intelligence is codominant;
3. discover that the distribution of intelligence in a population cannot be explained by Mendelian inheritance; and
4. become engaged in the idea that genetic and environmental factors influence behavior.

Preparation

Conduct this activity as a whole-class discussion.

- Refer to the *Teacher Background* for additional information related to the concepts of this activity.
- Prepare an overhead transparency of Copymaster 1.1, *Late Breaking News: Gene for Intelligence Discovered* (optional).
- Prepare an overhead transparency of a list of anonymous SAT or ACT scores (optional).

To assist the students with Question 4, try to obtain from the appropriate school official a list of anonymous SAT or ACT scores, preferably from a class of students that has already graduated.

Introduction

In this activity, the students begin to explore the inheritance of complex traits through the study of human behaviors. Notice that we have not chosen to use diseases as our examples of complex traits. This is because current human-genetics instruction focuses almost exclusively on rare, single-gene, Mendelian disorders, such as hemophilia (X-linked recessive); sickle-cell anemia and cystic fibrosis (autosomal recessive); and Huntington disease (autosomal dominant). This ignores the "normal" traits of interest to most students and, judging by news coverage, the media: aggression, sexual orientation, anxiety, risk-taking behavior, happiness, and intelligence, for example.

By focusing on normal traits, which demonstrate multifactorial causation and non-Mendelian inheritance, we hope to shift students' thinking to the world of genetics that the Human Genome Project is revealing. This is a world characterized by an increased understanding that populations possess an extraordinary range of genotypic and phenotypic variation, not a set of either/or genes and phenotypes. Behavioral variation is no exception.

Every person exhibits certain behaviors that are critical for life. The species maintains a pool of individuals who contain behaviors that help ensure survival and reproduction. For evolutionary reasons, it is helpful to the species if those behaviors occur naturally—that is, instinctually. For example, a newborn infant knows, without being taught, how to suckle to obtain milk. As development progresses, feeding behavior becomes more complex and its variations, such as using formal place settings, become more subject to learning and culture, but the feeding instinct remains. Thus, even though all of us experience the urge to eat, each of us maintains substantial control over the process of what, when, where, and how to eat. In this simple example, it is easy to see how biology (and ultimately, genes) and the environment (including experience) both play roles in this critical behavior:

Every person also exhibits behaviors that help define who we are but, at least in modern society,

may not play as direct a role in survival or reproduction. Intelligence, a quality of a person that behavioral geneticists consider to be a behavior, is highly prized in the United States. One reason is that high intelligence can help one to succeed in school, which often is the route to a lucrative job and a high standard of living. Those parameters may or may not aid survival and reproduction.

Intelligence is quite unlike suckling behavior, however, because its roots are not as obvious, nor are they as universally accepted. An infant does not spring forth with the attributes that most people would classify as intelligence, for example, the ability to speak several languages and do higher math. Instead, most people recognize that educational and cultural experiences are necessary to realize whatever inborn biological potential already exists. The degree to which biology sets the potential for intelligence remains a topic of heated debate.

In addition to previewing the genetic and environmental roots for all behaviors, intelligence also illustrates a ubiquitous feature of complex traits: their continuous phenotypic distributions. Even traits typically thought of as discrete Mendelian traits (in the sense that either one has the disorder or not), such as Huntington disease and cystic fibrosis, are not quite as discrete as most people think. There is considerable variation in the expression of those disorders among individuals. The students will explore continuous distributions of physical and behavioral traits in the second and third activities.

Process and procedures

Read the *Late Breaking News* article to the class or have each student read it quietly. Use the Analysis Questions to guide a discussion of some of the issues raised by the fictitious story. We are not looking for correct answers here because students have no foundation on which to build good arguments. Encourage an active discussion and accept all non-trivial answers. Ask students to challenge their peers' responses. Simply note the types of responses offered, paying particular attention to areas of misconception. Subsequent activities will offer opportunities to challenge students' thinking and will help them formalize accurate understandings of the factors contributing to human behavior.

We have structured the questions as a critical-thinking exercise, or inquiry. The first two questions are

designed to allow students to explore the concept of intelligence and allow them to express their understanding of this particular behavior and its measurement. The next three questions provide a review of Mendelian genetics, and remind students that they may know enough about genetics to evaluate the likely validity of certain science articles they read. For example, this article suggests that one gene with only two alleles acting in a codominant fashion could be responsible for intelligence. If that were true, only three phenotypes would result.

If you have an overhead of SAT or ACT scores, display it after the students have answered Question 3. Ask them to describe the range of scores and whether it supports the number of phenotypes predicted from the article. The list should show a wide variation in scores, and thus, a wide variety of intelligence phenotypes, which does not support the prediction.

In conducting this review of Mendelian inheritance, the students should discover two things: (1) they are capable of using their inquiry skills to discern the flaws in the fictional news report; and (2) some traits, such as intelligence, apparently do not exhibit Mendelian inheritance patterns. This last point will be expanded later in the module to teach continuous variation, polygenic inheritance, and multifactorial causation.

The last two questions ask students to list evidence that supports genetic and environmental contributions to human behavior. If the students have trouble coming up with evidence, guide them with more specific questions such as, What is the cause of Down syndrome (trisomy 21, genetic) or Can accidents or difficult births affect intelligence (environment)?

Notes from the field test: In several classes, there was a tendency for students to personalize their answers to Questions 6 and 7 (evidence for genetic and environmental influences on intelligence). For instance, students would talk about their own intelligence or the intelligence of parents, siblings, or other students. In some cases, the statements were mean-spirited, elitist, or even bigoted, inappropriately stigmatizing people based on socioeconomic status, personal likes or dislikes, or other factors. ("Genes determine intelligence because the kids in this gifted class come from smart parents with good jobs, but the kids from the trailer park are in the regular or dumb biology classes.")

"Environment makes a difference. I'm smart because my parents read to me, but they ignored my little brother. He's stupid.")

If you sense a negative or biased atmosphere developing in your classroom, defuse it quickly by reminding the students that scientific evidence must be unbiased. Teachers who kept the students focused on answering only the questions asked had the greatest success.

Extension ideas

One of the field-test teachers posed the following challenge to his students at the conclusion of this first activity: "Based on the activity you just completed, keeping in mind the questions that were posed, develop a hypothesis about what you will be learning in subsequent activities in this module." This question will encourage students to think more critically about the major concepts raised in the first activity and to practice using scientific-analysis skills.

Analysis questions

1. What is intelligence and how is it measured?

Students may define intelligence in many ways. Accept all reasonable definitions. For a comparison, you might read dictionary definitions, most of which include language about capacities to learn and solve problems. Behavioral geneticists use intelligence to mean general cognitive ability, which includes a variety of measures of specific cognitive abilities. Some educators recognize many different intelligences, such as verbal, visual, kinesthetic, musical, spatial, and mathematical. Howard Gardner's book *Multiple Intelligence: The Theory in Practice* (1993: Basic Books, New York) is one of the classic resources for this area of learning research.

Students also may realize that intelligence can be measured in formal and informal ways. IQ, SAT, and ACT tests are quite formal, but our peers also assess our intelligence, or their perception of our intelligence, on an informal and continuing basis.

2. How do our peers assess our intelligence?

Aside from formal measures, such as grades and test scores, students may mention any number of informal measures, such as the ability to

remember things like song lyrics, movie dialogue, or sports statistics. They also may mention special abilities with computers, writing, music, art, speaking ability, repairing car engines, and similar attributes.

3. **If the researchers' hypothesis is correct—that inheritance of intelligence is codominant—how many phenotypes you would observe in the population? What would the phenotypes be?**

Three phenotypes would be predicted. For example, if one allele specified high intelligence (H) and the other low intelligence (L), three genotypes and three phenotypes are possible. This assumes that there are no other influences on intelligence—genetic or environmental—and that all individuals in the population are in exactly the same developmental stage.

Table T1.1 Predicted Genotypes for Single-Gene Inheritance of Intelligence

Genotype	Phenotype
HH	High intelligence
HL	Intermediate intelligence
LL	Low intelligence

4. **Assume that a student's SAT or ACT score is a valid measure of that student's intelligence. If you reviewed a list of the SAT or ACT scores of all the juniors and seniors in your school, what would you find?**

Your guidance department might be able to supply you with SAT or ACT scores from past classes. This would be an improvement on just assuming that there would be a wide range of scores. A wide range of scores is to be expected. If the population of students is large enough and the scores were plotted on a graph, a bell-shaped curve could be expected.

5. **Do your school's test scores support the hypothesis that the inheritance of intelligence is codominant? Why?**

It does not support the hypothesis because the wide range of SAT/ACT scores indicates that there are many more phenotypes than the three that are expected from codominant inheritance. Continue the discussion so that students will discover that intelligence is not a trait like cystic fibrosis or Huntington disease, which breaks down as "either/or": either you have it or you don't. In the next activity, students will learn that intelligence, like height and novelty seeking, exhibits a continuous distribution. A continuum of intelligence or mental capacities is obvious, not only from the score data, but also from informal observations of their classmates.

6. **What evidence is there, if any, to suggest that genes contribute to intelligence?**

Students might respond that smart parents tend to have smart children or that people affected with Down syndrome (because they have a chromosomal [genetic] abnormality) are below average in intelligence. Other answers are possible.

7. **What evidence is there, if any, to suggest that the environment contributes to intelligence?**

Students may respond that blows to the head can impair the ability to think, lead poisoning contributes to mental retardation, and maternal drug abuse and even moderate use of alcohol during pregnancy can impair intelligence. Fetal oxygen deprivation during birth can result in low intelligence. Infants deprived of early learning opportunities, such as parents reading to them, seem to enter school with greater challenges to learning than children with rich learning environments. Many similar responses are possible.

Activity 2

Human Variation

Overview

In this activity, students learn that some traits are characterized by continuous variation, which often is due to the effects of multiple genes and environmental factors. That is in contrast to qualitative or discrete variation, which generally arises from the effects of single genes. Emphasize that the vast majority of human traits, normal or abnormal, have a multifactorial origin. Students will discover that multiple genes can influence the development of the complex trait of height and can help explain individual differences in this trait in a population. They also will discover that environmental factors can influence height to increase the wide range of phenotypes further. We begin the treatment of continuous variation with a physical trait because students can accept readily that genes influence height. The transition to behavior will be easier if the underlying principle (genes and environment influence complex traits) remains the same and only the trait changes.

Major concepts

- Many traits are characterized by continuous variation.
- Qualitative or discrete variation often arises from single gene effects.
- Continuous variation may result from the combined effects of multiple genes and environmental factors.
- Height displays continuous variation.
- Height is affected by genetic and environmental factors.

Estimated time

50 minutes

Learning outcomes

In this activity, the students will

1. become aware that certain traits show continuous variation rather than discrete variation;
2. model polygenic inheritance and multifactorial causation (avoid the term multifactorial *inheritance* even though it is used in many texts; it includes environmental factors, which obviously are not inherited);
3. generate data and prepare graphs that show a continuous distribution in heights; and
4. relate variation in height to both genes and environment.

Preparation

- Prepare an overhead transparency of Copymaster 2.4, *Modeling Genetic and Environmental Influences*.

Materials

(per class of 30, students working individually)

- small beads, such as pop beads: 150 each of red and white and 30 each of orange, yellow, green, and blue
- 60 plastic film canisters, with hole punched in lid: 30 labeled "Mother" and 30 labeled "Father"
- 30 paper or plastic cups
- 30 copies of Copymaster 2.1, *Human Variation Worksheet—Female*
- 30 copies of Copymaster 2.2, *Human Variation Worksheet—Male*
- 1 copy of Copymaster 2.3, *Histogram Template for Heights*

You can purchase pop beads from Ward's Natural Science Establishment, Inc. (catalog #36V1530 to 36V1531 and #36V1533 to 36V1536). Alternately, you can use colored paper clips or jelly beans.

Introduction

Genetics can be defined as the study of the inherited components of phenotypic variation. This activity allows students to consider the factors that influence phenotypic variation by examining the trait of height. To begin to make the point that variation can be continuous as well as discrete, we first ask students to assume that the inheritance of height follows codominant Mendelian patterns and is due to a single, two-allele locus. (They did the same thing in Activity 1 with the trait of intelligence.) They should recognize that under these circumstances, the number of phenotypes possible in the suggested scenario is three (tall, medium, and short). It should be obvious that the distribution of student heights in their own class does not fit this simple Mendelian pattern.

To explore alternative genetic explanations, the students conduct an activity using beads that model the distribution of heights that would result if six genes influence height rather than one. As they explore the example of **polygenic** influence, the students also

investigate **multifactorial** (genetic factors plus non-genetic factors) influence by considering how the environment can affect height.

In genetics, environment refers to anything that is not genetic, such as family, school, and diet, as well as unknown sources of variation. In addition, the concept of development is introduced—genes are being turned on and off throughout the life cycle and the same environmental factors may have different effects at different stages of development. Alcohol is a good example. When ingested by a pregnant woman, it may damage the developing fetal brain and many other parts of the body, resulting in fetal alcohol syndrome. Alcohol's effects on people later in life are well-known and are the subject of Activity 5.

Although we take the students through this exercise with the genetic contribution first and then follow it with the environmental contribution, which produces the final height, you should realize that this is artificial and done only for simplicity. In reality, genes cannot operate in an environmental vacuum, and the environment cannot exert an influence on genes in their absence. Genes and environment are inextricably linked. That point is emphasized in the reading at the end of the activity.

Part I: Modeling Genetic Influence

Process and procedures

To demonstrate a continuous distribution of heights, it is desirable to have measurements from a large number of individuals. Thus, students will work individually to model height, rather than in teams. They will model how six genes affect the height of a population of females, and then males, to discover that multiple genes produce a continuous distribution in each population that is more consistent with observed heights than is the single-gene model considered in the introduction. (Optional: If you choose to combine both male and female populations, the range of continuous variations may become a bit bimodal because of the differing effects of sex on height, but the distribution still should be continuous.) The various combinations of two alleles at six different genetic loci produce a large distribution of heights. Later, you may have to help the students contrast that with the introductory scenario in which

only one gene, with codominant expression from two alleles, gave rise to just three heights.

Because the sex chromosomes have an influence on height, students will compensate for this difference by assuming that a population of females has a starting height of 165 cm and a population of males has a starting height of 175 cm. Have the students first model the heights of a female population, then repeat the process for a male population.

Steps 1–8. To begin, place ten beads (five red, five white) into each of thirty cups. Have each student withdraw four beads, two at a time, from his or her cup; the students should select randomly. The first two beads are placed into a film canister labeled "Mother" and the second two are placed into a second canister labeled "Father." Have each student shake the parental containers and pour out a single

bead from each to provide a pair of alleles for the first gene. Each student should record his or her allele combination in the space next to "Gene 1" on the *Human Variation Worksheet—Female*.

In preparation for selecting the alleles for the second gene, instruct the students to empty all four of their beads back into their cup after recording the data. Have the students repeat this process five times—first selecting four parental alleles and then two off-

spring alleles—until they have recorded allele combinations for all six genes.

Finally, have the students use the same procedures to model and record data for a male population. Once again, each student should begin with a cup containing five red and five white beads. Wait until the students have finished Part II before giving them the numerical values of the "gene" beads.

Part II: Modeling Environmental Influence

Process and procedures

Steps 1–6. This section adds an environmental component to the calculated final height after genetic influences are totaled for both sexes. This time, however, the beads represent environmental factors, not alleles. Remind the students that this separation in time of genetic and environmental influences is an artificial one imposed by our modeling process and that in the real world genes and environment exert their effects simultaneously. The students also must keep in mind that a given environmental factor can influence growth (and other human traits) differently at different stages of development.

For this part, development is divided into three stages: prenatal, childhood, and adolescence. Although environmental influences are not packaged in discrete units like genes, we will use colored beads to represent "factors," which can be thought of as packets of environmental influence. Provide each student with a film canister containing one orange, yellow, green, and blue bead. Have each student shake the canister, pour out a single bead, and record its color in the space labeled "Prenatal" on the *Human Variation Worksheet—Female*. Ask students to replace the bead and then repeat the process to obtain colors for "Childhood" and "Adolescence." The students use the same procedure to obtain comparable data for the male population.

Once the students have completed the data collection for both Parts I and II, give them the values for the colors associated with the genes and environmental factors as listed in Copymaster 2.4, *Modeling Genetic and Environmental Influences*.

Data organization

Step 7. Use Copymaster 2.3, *Histogram Template for Heights*, to organize the two sets of data. Alternately, you can simply draw a horizontal line on a chalkboard or an overhead transparency with increasing height ranges from left to right. To see a bell-shaped distribution, group heights in ranges of 10 cm (for example, 180 to 190 cm). Students place an X above the line at a position corresponding to their calculated final height range (starting height + genetic + environmental effects). As more students add their Xs to the same height range, they place their X above the preceding one, building up a histogram. To save time, use an overhead transparency or chalkboard and ask students to call out their heights as you record them.

Remind the students to read the section *Additional Information about Height, Genes, and Environment* that follows the Analysis Questions. This discussion will help them answer Questions 7 and 8.

Analysis questions

1. What are you simulating by withdrawing four beads from the cup in Part I?

The four beads represent the parental alleles (two from each parent) for each gene being modeled. This initial selection is designed to produce variation in the parental genotypes.

2. Why must you withdraw a pair of beads six times?

This activity assumes that height is affected by six different genes, in addition to the sex chromosomes. To model that influence, you must select six pairs of beads (six pairs of alleles).

3. Describe the distribution, or range, of heights on the class graph. Does the distribution reasonably model actual distributions of height? Explain.

Even though class results will vary, there should be a relatively continuous distribution of heights. This continuous distribution should more accurately model the actual distribution as compared to the discrete Mendelian patterns suggested in the introduction.

4. Does a single-gene or multifactorial model better explain the inheritance of height? Why?

The multifactorial model better explains the inheritance of height because it predicts a continuous distribution of heights that reasonably matches the observed heights, whereas the single-gene model predicts just three discrete heights.

5. What type of variation is evident in the class data? What explains this variation and how does it differ from the variation seen in blood types?

The class data show continuous variation due to the influence of multiple genes and environmental factors. These effects are additive. This is in contrast to blood groups, which display discrete variation.

6. If you were to combine the data from your class with the data from several other classes, how would the graph of height change? Would the graph provide a better or worse illustration of a continuous variation? Why?

Combining the data from several classes will yield a larger sample, which should give a smoother and more complete distribution of heights. If female and male data are combined,

the distribution may appear bimodal. That, too, is a continuous, though more complicated, distribution.

- 7a. What biological factors influence growth? How are those factors related to or influenced by genes?

Many biological factors controlled by genes are important for growth. For example, hormones influence growth. Students may be aware of growth hormone, which is formed in the pituitary gland and, obviously, influenced by genes. Underproduction of growth hormone can cause dwarfism; overproduction may lead to a form of gigantism known as acromegaly. Other hormones that influence growth include insulin, thyroxine (thyroid hormone), and sex hormones. In addition, the dozens if not hundreds of genes that contribute to the complex structure and development of bone, and the myriad of genes that controls rates of metabolism in general, all make genetically controlled contributions to adult height.

- 7b. What environmental factors interact with genetic factors to influence height?

No matter what a person's genetic "thermostat" was set at when fertilization occurred, that height will not be achieved if that individual grows up under starvation conditions. Prenatal effects, including exposure to maternally ingested alcohol and cigarette smoke, or severe nutritional deprivation, may result in infants who have low birth weights and short stature. Even in North America, junk food diets and minimal protein intake during childhood and puberty can impair growth and lead to shorter adult height than specified by the person's genotype. Chronic infection in any organ system of the body also may impede growth through mechanisms that are not understood.

Activity 3

A Novel Trait

Overview

In this activity, students learn that there is variation in behavioral traits just as there is variation in physical traits such as height. They will accomplish that by completing a mock novelty-seeking survey and then assessing the range of class scores by graphing them. Novelty-seeking behavior has been shown to have a significant genetic component, although the environmental influences are even stronger. The actions listed in our survey are not drawn from any real or validated test and, thus, will not assess real behavior. They are meant to survey students' *tendency* to take risks and to illustrate continuous distribution.

In addition, this activity will begin to build the students' understanding that scientific methods can reveal the genetic and environmental contributions to complex behavioral traits. To do that, they will compare the novelty-seeking scores of identical and fraternal twins. This twin analysis will introduce the students to one of the most fundamental methods that behavioral geneticists employ to study genetic and environmental contributions to behavior. Moreover, we will ask the students to think about the limitations of such methods, for example, the difficulty of defining and measuring behavioral phenotypes.

Major concepts

- There exists variation in behavioral traits just as with physical traits.
- Novelty-seeking behavior has a genetic component.

- Novelty-seeking behavior has an environmental component.
- Behavioral geneticists use twin studies to investigate the genetic and environmental contributions to behavior.

Estimated time

50–75 minutes

Learning outcomes

In this activity, the students will

1. recognize that there is variation in human behavior;
2. understand that genes *and* environment influence human behavior;
3. analyze a twin study to learn that scientists can investigate the genetic components of behavior; and
4. appreciate that the methods of behavioral genetics, like other scientific methodologies, have certain strengths and limitations.

Preparation

- Prepare an overhead transparency of Copymaster 3.3, *Scatterplot of Height for Identical Twins*.
- Prepare overhead transparencies of Copymasters 3.2, *Scatterplot of Novelty-Seeking Score Data for Identical Twins*, and 3.5, *Scatterplot of Novelty-Seeking Score Data for Fraternal Twins* (optional).

Materials

(per class of 30, individuals and teams of two)

- 30 copies of Copymaster 3.1, *Novelty-Seeking Survey*

- 30 copies of Copymaster 3.4, *Novelty-Seeking Score Data for Fraternal Twins*
- 30 slips of blank paper, identical
- 60 sheets of graph paper
- 1 hat, bucket, or other opaque container

Note: This survey is not a valid measure of any actual behavior. It was constructed solely for educational purposes. If you suspect, however, that parents or administrators might be concerned about some aspect of this activity, follow appropriate procedures to gain their permission.

Part I: Novelty-Seeking Survey

Process and procedures

Step 1. Distribute the *Novelty-Seeking Survey* (Copymaster 3.1) and instruct the students to complete it quickly and without discussion. Remind the students to answer the questions on both pages of the survey. To maintain confidentiality of student responses, make sure that they do not write on the survey itself, but rather keep a tally of their "yes" answers on a separate piece of paper.

Steps 2-3. Once the students have counted the number of "yes" responses on their surveys, distribute the identical slips of blank paper. Have each student record his or her total on the paper, fold it once, and place it in a hat or other opaque container.

Step 4. Ask students to predict how they would expect a class profile of scores to appear. Would they

expect everyone to have the same score, scores at one extreme or the other, or relatively equal numbers of several scores? The answers that students offer will give you some indication of their understanding, or lack of understanding, that many complex phenomena produce a bell-shaped distribution when graphed.

Next, have the students test their predictions by graphing the survey scores. On the chalkboard, construct the axes of a graph to display a histogram of the number of students (y-axis) versus scores (x-axis). Depending on the range of scores and the size of your class, the scores probably should be reported in groups of three to five. Figure T3.1 shows a sample histogram. This will increase the chance that a bell-shaped distribution will be apparent.

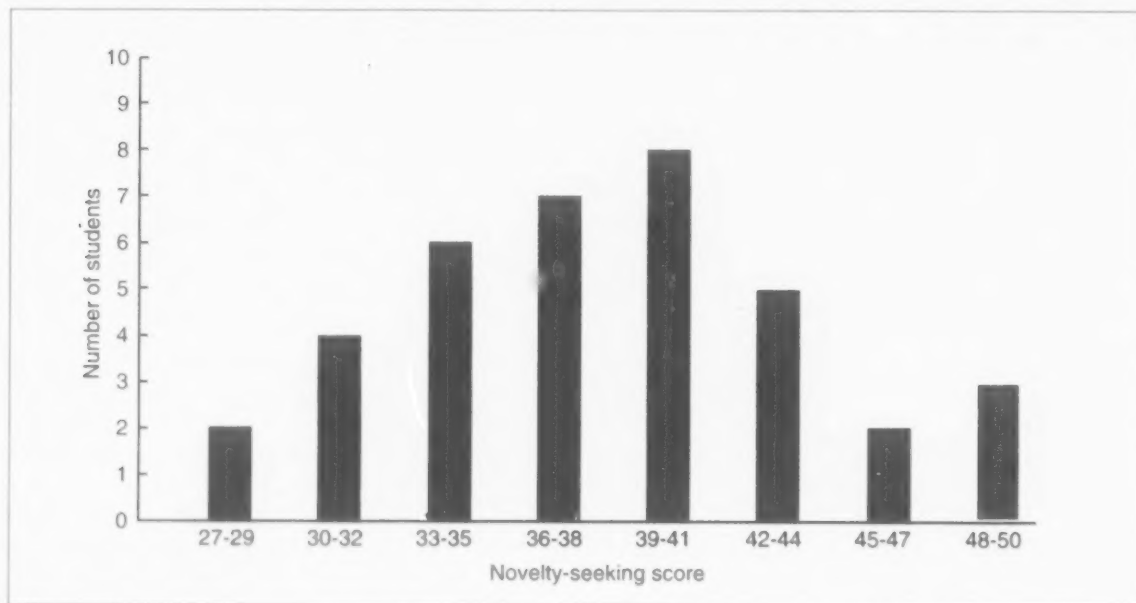


Figure T3.1 Sample histogram of novelty-seeking results.

Involve students in creating the histogram by directing each student to choose randomly a slip of paper and to record the value on the graph by placing a small horizontal line in the appropriate place. For example, the third student to select the score of 35 from the hat would place his or her small mark above the 33–35 indicator on the x-axis and directly across from the number 3 on the y-axis. Once all the scores are reported, create histogram bars by extending the highest marks at each score interval down to the x-axis.

Part I analysis questions

1. Describe the distribution of scores (the shape of the graph). *Hint: What is the approximate average score? Did everyone have the same score? What type of variation is evident?*

In the best case, the distribution will approximate a bell-shaped curve centered around the mean (average). In any case, the distribution likely will be continuous; thus students should recognize this type of variation as more similar to that for height than for blood type. Students should notice that there are relatively few individuals with extremely high or low scores and many more in the midrange.

2. How might you explain that distribution of scores?

For the trait of novelty seeking, students likely will identify various environmental influences such as culture, family environment, or peer group, as potential explanations for the observed distribution. A person might work in a job where risk taking is a part of everyday life, for example, a miner, fisherman, or policeman, or he or she might live in a risky place or climate, such as a mountainous area, very cold region, or region with hurricanes. Age also is a common response, although by itself, age is insufficient because people of all ages engage in some level of novelty-seeking behavior and the students are observing variation among peers of roughly the same age. Students who make the following extrapolation—that continuously distributed behavioral traits may have similar causes as continuously distributed physical traits—might suggest that genetics influences risk taking.

3. Do you think the survey is an accurate way to measure the risk-taking (or novelty-seeking) aspects of an individual's personality? Why? If you answered no, suggest a better measure.

Surveys like these (and these are NOT actions from a real survey) are used to evaluate personality traits and are a routine part of some job-matching exercises. Nonetheless, students are justified in disputing the actions as trivial or too risky and in calling into question the validity of the survey as a novelty-seeking measure. One intent of this question is to get students thinking about the limits and strengths of methodologies used in behavioral genetics. Make clear to the students that real surveys of novelty seeking are quite accurate and reliable (relative to how psychiatrists define novelty seeking) because they have been evaluated extensively for validity and reliability.

4. Think back to the height analysis that you performed earlier. How did you explain variation in height?

When students reflect on the previous height activity, they should recall that parents' heights are associated with children's heights. Even more obvious, perhaps, is the role that one's genetic sex plays on height: females have a predicted adult height 10 cm shorter than males. These relationships clearly have a genetic component involving more than one gene. For height, the environment also can play a strong role. That can be observed by the effect of nutrition, for example, where poor diets can result in short stature.

5. Is it reasonable to propose that we can explain variation in personality traits the same way we explain variation in height? Explain.

Students may answer in a variety of ways, but many are likely to say that novelty-seeking behavior is different from height because novelty seeking is not physical. Other students may acknowledge that the type of continuous variation seen in novelty seeking is similar to that in height and, thus, might have similar multifactorial roots. Others may be aware of news reports that link genetics and behavior. The remainder

of the activity will establish a relationship between genetics and behavior, in this case, the personality trait of novelty seeking.

6. **Do you think your total score would be different if you took the survey at ten years old or forty-five years old?**

Behavioral traits, like many other traits, are not necessarily static—they can change across time. For example, an individual's height

varies by age not only through normal childhood growth but also through some decrease in height in the elderly. Novelty seeking might also be expected to increase during childhood, peak during adolescence or young adulthood, and slowly decrease across time for the remainder of the lifespan. The implications of those changes are that genetic and environmental influences are not static but may be regulated by the processes of development throughout the lifespan.

Part II: Data from Minneapolis-St. Paul Study

In this part of the activity, the students will discover that a physical trait (height) and a behavioral trait (novelty seeking) are more similar between identical (monozygotic, MZ) twins than between fraternal (dizygotic, DZ) twins. Because identical twins are genetically identical and fraternal twins share only 50 percent of their genetic material (on average), such studies can provide evidence in support of the role of genes in behavior.

Process and procedures

Step 1. Identical twins are genetically identical, which makes them interesting biological subjects for studies of anything suspected of having a genetic basis including diseases, simple traits, or complex physical or behavioral traits. If identical twins are very similar for certain traits, then it is reasonable to test whether identical genetics might be one reason.

Step 2. In general, we would not expect identical twins who are adopted and raised apart to share the same environmental influences. That is significant because if identical twins are raised in the same household, it is very difficult to separate genetic from environmental (family/rearing) effects. Adopted-apart twins allow scientists to estimate how much genes might influence behavior.

Step 3. Such a list might include facial features, height, taste in foods, personality, shoe and clothing size, eye and hair color, time of onset of puberty, voice quality, and speed and strength. Students may notice that most of those are more physical/genetic than environmental. In fact, it is difficult to think of things that fraternal twins would be more likely to share than identical twins.

Step 4. If students believe that genetics is important in novelty seeking, they should expect the adopted-away identical twins to have scores similar to their co-twins. If they believe environment to be most important, they should predict a range of scores that does not correlate closely between twin pairs.

Step 5. Students should propose administering the same survey to the co-twins.

Steps 6–7. If your students have reasonably good graphing skills, allow them to graph the scores of the identical twin pairs. If the students' graph-making skills are poor, display an overhead transparency of Cypmaster 3.2, *Scatterplot of Novelty-Seeking Score Data for Identical Twins*, which shows that few scores are below 35, few are above 41, and most cluster in the middle range. Students should notice scores of identical co-twins are similar. In addition, there is a slight but noticeable clustering around the diagonal extending from lower left to upper right, which suggests a positive correlation.

Step 8. Students should predict a close correlation between the heights of identical twins.

Step 9. Display an overhead of Cypmaster 3.3, *Scatterplot of Height for Identical Twins*, and use it as the focus of discussion. Students should respond to the questions by noting that most heights are between 165 and 180 cm, and the heights between most identical twins are very similar. There is an obvious tendency for points to cluster around a diagonal line, which is evidence of a strong positive correlation. The correlation is stronger for height than for novelty seeking.

Step 10. Students most likely will suggest that fraternal twins will be less similar in height and novelty seeking than identical twins. They should note that if genes are important for influencing height and novelty seeking, less genetically similar twins (fraternal twins) should be less similar phenotypically.

Step 11. Distribute Copymaster 3.4, *Novelty-Seeking Score Data for Fraternal Twins*, and direct the students to graph those data to test their predictions. If you choose not to have the students generate their own graphs, display an overhead of Copymaster 3.5, *Scatterplot of Novelty-Seeking Score Data for Fraternal Twins*.

Part II analysis questions

Use the Analysis Questions, the students' graphs, and the overhead graphs to conduct a discussion with the class. To further the students' understanding of the activity, instruct them to read the section *Additional Information about Novelty Seeking, Survey Methods, and Scatterplots*.

1. Compare the heights for the fraternal twins. What similarities and differences do you notice when you compare those data with the data from the identical twins?

The students should notice that the heights of the identical twins correlate more closely than the heights of the fraternal twins. A side-by-side look at the two graphs shows clearly that there is substantially more variability around the straight line for fraternal twins than for identical twins. The actual correlations represented by the scatterplots for identical and fraternal twins are 0.97 and 0.61 respectively.

2. How would you explain the similarities and differences?

The greater similarities in heights of identical twins must be due largely to genetics because adopted-away twins (identical or fraternal) do not share the same environment. The differences may be environmental or genetic or both; it is difficult to assess.

3. Compare the novelty-seeking graphs for the identical and fraternal twins. What similarities and differences do you notice?

As with height, the scores of the identical twins appear to correlate more closely than the scores of the fraternal twins, but overall the novelty-seeking scores are not as highly correlated as the height measurements. In fact, the correlation for identical twins is 0.60 but only 0.23 for fraternal twins, a very weak correlation.

4. Would you explain the similarities and differences the same way you did for height?

It is reasonable to conclude that similar mechanisms influence novelty-seeking behavior and height because a similar relationship seems to exist between the data of identical twins and fraternal twins. Thus, the greater similarity between identical twins probably is related to their greater genetic similarity.

5. Based on these data, is it reasonable to conclude that genes influence height? Explain your response. Based on these data, is it reasonable to conclude that genes influence novelty-seeking behavior? Explain your response.

Because the environments were different for both sets of adopted-away twins, we can conclude that the environment probably contributed very little to the similarities in height for both identical and fraternal twins. The correlation difference between identical and fraternal twins, on the other hand, strongly suggests that genes influence height. The significant testable variable in the height study is the amount of genetic similarity between the twins. Adopting away controls for environmental bias. Identical twins share all their genes whereas fraternal twins share only half, on average. If genes are a factor in height, it is reasonable to expect greater correlation between the heights of identical twins. That is what we observe. The same also appears to be true of novelty-seeking behavior, although the amount of genetic influence, as reflected in the strength of the correlations, seems to be weaker.

6. Based on these data, is it reasonable to conclude that the environment influences height? Explain your response. Based on these data, is it reasonable to conclude that the environment influences novelty-seeking behavior? Explain your response.

Because all identical twins are not perfectly identical in height or novelty seeking all the time, genes are, by definition, not the only factors affecting those traits. Thus, it is reasonable to conclude that the environment influences both traits in both twin types. It should be noted that height for identical twins is largely determined by genes. It should also be apparent that environmental influences are stronger for novelty seeking than for height. That is indicated by the lower correlations for novelty seeking between both types of twins.

7. Based on the phenotypic variation that you observed for the personality trait of novelty seeking, would you expect one or more genes to be involved? Explain.

If students understood the message of the activity on human variation, namely, traits that show continuous variation (quantitative variation) usually are influenced by several genes, then they should respond that many genes probably influence novelty seeking. If only one gene, with perhaps two or three alleles, was responsible,

we would expect that the class and twin scores would fall into just a few discrete categories.

8. If you agree that novelty-seeking behavior is affected by genes and the environment, you agree that novelty seeking is a multifactorial trait. What environmental factors might affect novelty seeking?

The novelty-seeking behavioral tendencies of friends; interest in sports; the stability of life at home; and access to novel activities (for example, ski slopes, white-water rafting), to name a few.

9. Is it likely that novelty seeking is unique, or would you also expect other human behaviors also to be influenced by genes? If yes, which behaviors?

There is no reason to expect that novelty seeking is unique among human behaviors. Thus, it is likely that genes and environment would influence other behaviors as well, such as happiness, depression, anxiety, tendency to abuse drugs, and intelligence.

Activity 4

Finding the Genes That Influence Novelty-Seeking Behavior in Humans

Overview

In this activity, the students will move from understanding that behavioral geneticists can use twin studies to ascertain that there *are* genetic contributions to behavior, to searching for the genes themselves. It is this type of study that often leads to the "Gene-for-X-found" headlines that may be familiar to the students. The students will model a gene-association study similar to the one that scientists used to identify a region of chromosome 4 that is associated with a resistance to developing alcoholism. In this activity, students work with two hypothetical genes, *CTM1* and *RCM3*.

Major concepts

- Association studies have identified genes associated with human behaviors.
- Individual genes associated with human behavior typically have a small impact on the overall behavior.
- Genes associated with a behavior are often thought of as determining a behavior; in fact, they merely influence it.
- DNA sequences identified in association studies are often not in the gene itself, but rather are located close by.
- Functional genomics can be used to assess whether a candidate gene is more or less likely to play a role in the behavior being studied.

Estimated time

50 minutes

Learning outcomes

In this activity, the students will

1. understand one of the methods (gene-association study) that behavioral geneticists use to investigate the genetic basis of variation in human behaviors;
2. appreciate the strengths and limitations of that method;
3. review the principles of Mendelian inheritance and transmission genetics;
4. learn about (or review) the techniques of PCR and gel electrophoresis; and
5. have the opportunity in an extension activity to learn basic statistical methods.

Preparation

- Prepare 8 copies each of Copymasters 4.1, 4.2, 4.3, and 4.4, *Research Subjects: Genotypes and Novelty-Seeking Scores*. If you have more than or fewer than thirty students, prepare enough copies so that each student can analyze five research subjects and all twenty research subjects are represented in the class.

Materials

(per class of 30, individuals and teams of two and four)

- 1 copy of Copymaster 4.1, *Group 1A Research Subjects: Genotypes and High Novelty-Seeking Scores*
- 1 copy of Copymaster 4.2, *Group 1B Research Subjects: Genotypes and High Novelty-Seeking Scores*

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- 1 copy of Copymaster 4.3, Group 2A Research Subjects: Genotypes and Low Novelty-Seeking Scores
- 1 copy of Copymaster 4.4, Group 2B Research Subjects: Genotypes and Low Novelty-Seeking Scores
- 30 copies of Copymaster 4.5, Gel Template Sheet
- 30 copies of Copymaster 4.6, Graph Template for Novelty-Seeking Score Data
- 1 copy per team of Copymaster 4.7, Histogram Template for Allelic Frequencies
- 30 copies of extension material (optional)
- 1 hat, bowl, or other suitable container

Introduction

A gene-association study similar to the one modeled here found an allelic polymorphism putatively linked to novelty seeking. (That finding was supported by the independent work of two labs, Benjamin et al. [1996] and Ebstein et al. [1996]. Researchers have used similar methods to identify genes possibly involved in other human behaviors. A significant point here is that even though individual genes may exert only a minor influence on certain behaviors, powerful molecular and statistical techniques, when properly applied, still may allow behavioral geneticists to detect their effects.

Unfortunately, this great power of detection can have negative consequences. Even though many other genes (as well as environmental factors) also may be required to produce the behavior under consideration, the identification of *any* single gene often gets interpreted as the *only* gene. That leads to the misconception that genes *determine* behavior rather than *influence* behavior. In addition, association studies, such as the one modeled here, only identify *DNA sequences associated with a trait*. The sequence may be located within the gene itself or perhaps just very close to it. Additional methods are required to test whether the candidate gene directly influences a behavior.

Once a candidate gene has been associated with a particular behavior, scientists try to establish whether a similar gene already has been identified in another organism. If so, the gene's function in a model organism may offer clues to the gene's function in humans. For example, if a human gene thought to be associated with novelty-seeking behavior is similar to a gene in *Drosophila melanogaster* involved in neurotransmission, then it is plausible that the candidate gene exerts an effect in the brain, which is the organ of behavior. On the other hand, if the human gene is similar to a

Drosophila gene that codes for a structural protein, then the association becomes more dubious. This process of comparing DNA sequences from model organisms to humans helps scientists understand the function of human gene products and is known as functional genomics.

Scientists can obtain data for gene-association studies using the polymerase chain reaction (PCR). If necessary, review the theory of PCR and gel electrophoresis with your students prior to beginning this activity. The genes used in this study are fictitious but could represent neurotransmitter genes, which are candidates for playing a role in novelty-seeking behavior. The names *CTM1* and *RCM3* reflect a convention in naming genes with abbreviations derived from the full gene name (for example, cortical neurotransmitter might be **CTM**) and with an attached number if more than one gene of the same general type is known.

In this activity, models of PCR and gel electrophoresis are used to detect length differences of the *CTM1* and *RCM3* alleles. These length differences are due to the number of copies of short repeated sequences found in the middle of each amplified region. These variations are called short tandem repeat polymorphisms (STRs) and are the same types of repeats found in some genes associated with disease, such as Huntington disease or fragile X syndrome. Those disorders are caused by a great increase in the normal number of trinucleotide repeats found within those genes. The presence of the extra repeats leads to a nonfunctional gene product. For *CTM1*, the repeat is a CA (a dinucleotide) and for *RCM3* the repeat is AGT (a trinucleotide).

You also should be aware that, unlike the activity described here, most gene-association studies do not involve DNA polymorphisms from the target gene itself. Instead, the polymorphisms are located at a specific chromosome location near the gene of interest. Such polymorphisms are called markers and can reliably point toward the target gene. However, markers must be positioned sufficiently close to the target gene so that they are rarely separated by recombination, that is, the markers must be linked to the target gene.

Process and procedures

Step 1. Place folded copies of Copymasters 4.1–4.4 in a container. Allow each student to select one

sheet, which represents genotype data and novelty-seeking scores for five research subjects. Make certain that all twenty research subjects are represented among the students in your class.

Step 2. In this step, it is critical that students count the number of bases in each allele accurately. (An odd number of bases for the *CTM1* gene is a sure sign that students have miscounted, as is an even number for *RCM3*, except for the 58 allele.) Suggest that they write the size of each allele directly on the copymaster, next to the appropriate allele. That will help them to avoid forgetting the sizes before drawing the positions of the alleles on the *Gel Template Sheet*. If students have difficulty understanding how to record the position data on the gel, demonstrate the process on one of the alleles. Figure T4.1 shows a completed gel template.

Students should be able to count all their alleles and record their positions on the gel in 15 to 20 minutes.

Note: For simplicity, we give the students only a single strand of DNA for each allele. Make certain that they understand that DNA is double stranded in its natural state. Also, even though we refer to the DNA sequences as "alleles" or "genes," students should realize that in reality such sequences are just short markers within much longer genes. Finally, some research subjects are homozygous for a particular allele (1, 3, 5, 9, 13, and 15 for *CTM1* and 2, 6, 7, 12, 14, and 20 for *RCM3*). Thus, they display only a single band. When students count allele frequencies in Step 6, you may need to remind them to count each of these single bands as two alleles.

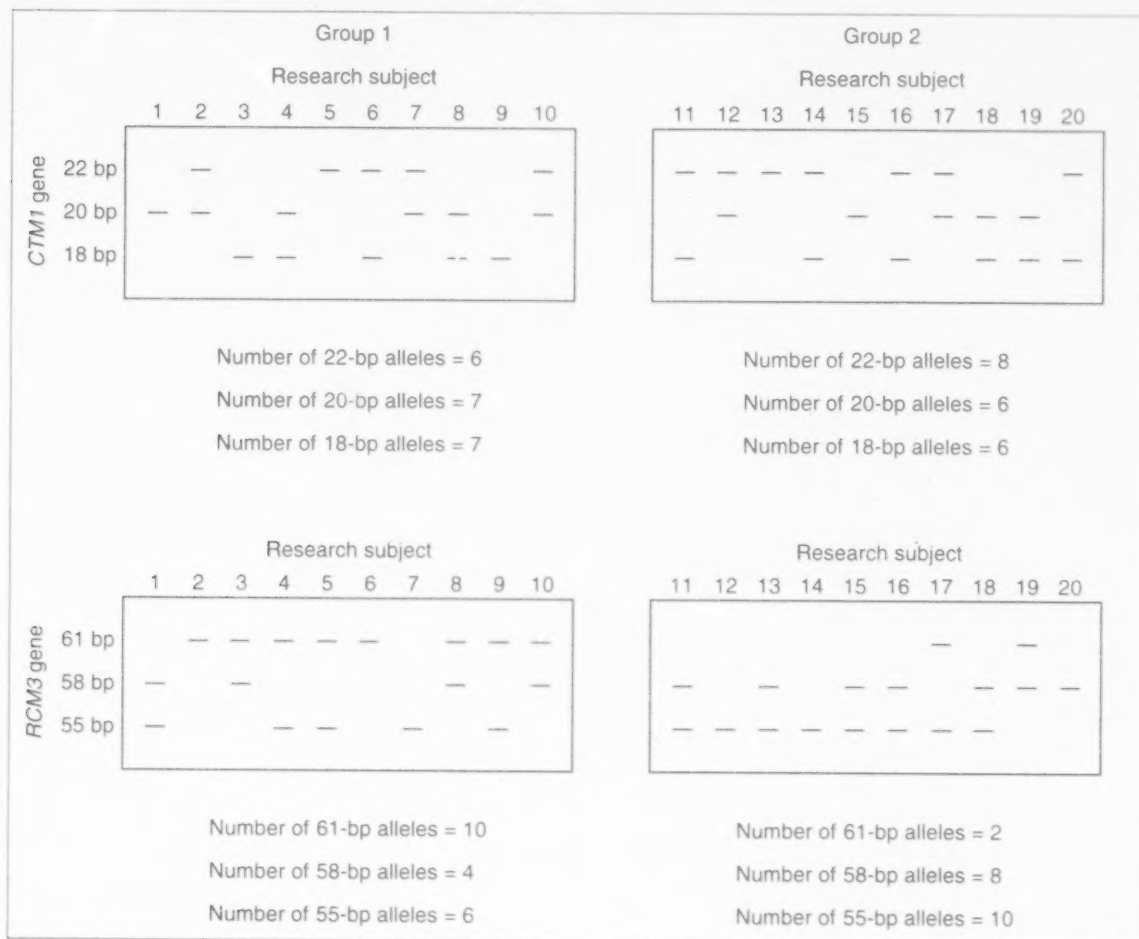


Figure T4.1 Completed gel template sheet.

Step 3. Each student should plot the novelty-seeking scores of his or her five subjects, using the *Graph Template for Novelty-Seeking Score Data* as a guide. If you would like to place more emphasis on graphing skills, have the students create their own graphs, including labeled axes, instead of using the template provided.

Steps 4–5. The purpose of forming teams in these steps is to ensure that all students acquire a complete data set. First, the students should form teams of two that complete a group. For example, a student with Group 1A research subjects would partner with a student who has Group 1B subjects. Within each group, all subjects are either high novelty seekers (Group 1) or low novelty seekers (Group 2). (Students will discuss the selection of groups once complete data sets have been assembled.) Next, students should form teams of four that complete all

twenty research subjects. For example, two students from Group 1 join with two students from Group 2. At each step, each student should record all data collected by his or her teammate(s), including genotypes (as represented by bands on the gel) and novelty-seeking scores (as recorded on the graph).

Step 6. Because all students now have a complete data set, they may return to working as individuals, or you may decide to allow them to continue working in teams of two or four. To plot the frequency of allele types, students first must count the number of alleles at each size according to their gene type (*CTM1* or *RCM3*) and group number (1 or 2). The number of alleles is determined by counting from the gel the number of bands at each size (remembering to count bands representing homozygotes as two). For example, if the students begin with allele 18 of *CTM1*, they will find seven copies of the allele

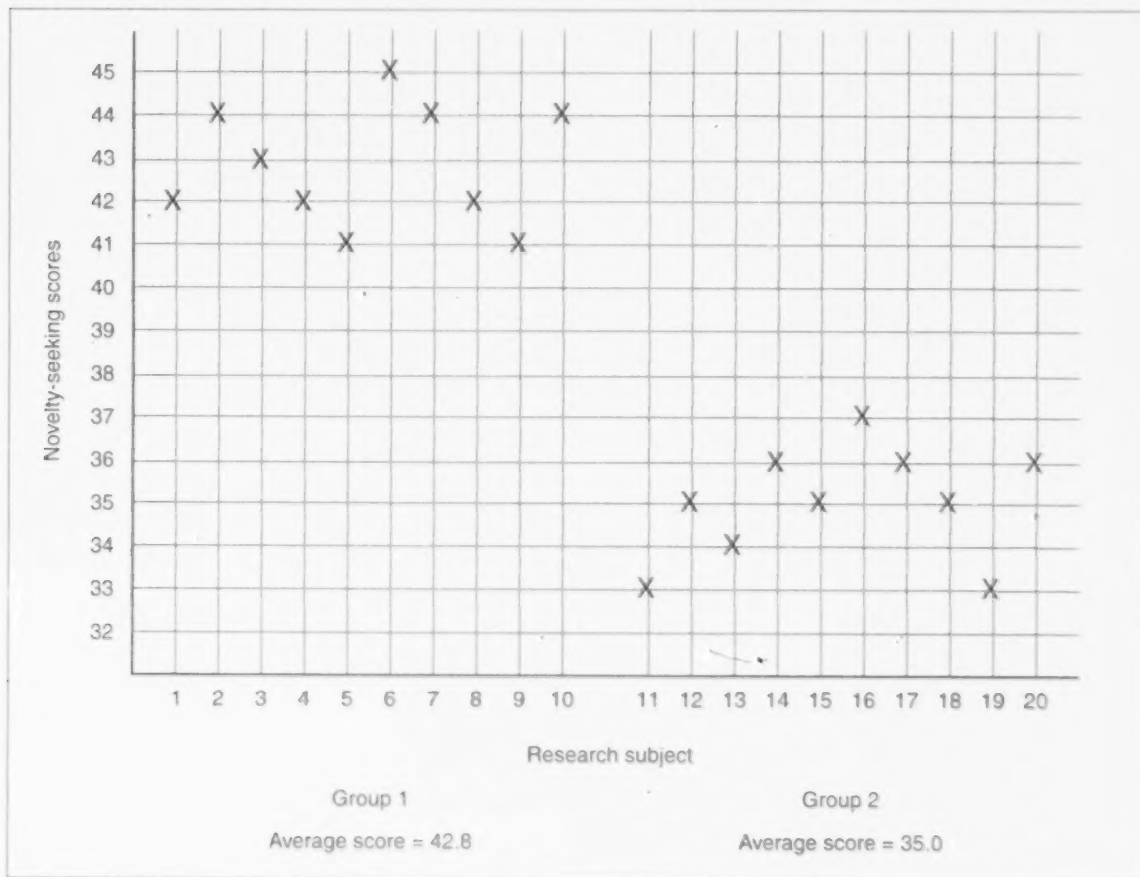


Figure T4.2 Completed graph of novelty-seeking score data.

among Group 1 subjects and six copies among Group 2 subjects. These frequencies should be plotted as two bars (one for each group), side-by-side, above the label "18" on the x-axis of the *Histogram Template for Allelic Frequencies*. The y-axis displays a scale indicating the number of alleles. (Again, if you choose to emphasize graphing skills, allow the students to create their own histograms.) The average novelty-seeking score for Group 1 is 42.8; the average score for Group 2 is 35.0. This will be important during the analysis.

Analysis questions

1. Can DNA polymorphisms that lie outside the coding regions of genes be useful to scientists hunting for genes that influence behavior?

This question helps students realize that the DNA investigated in an association study need not be a gene itself to be useful in ascertaining whether a particular gene may influence a trait.

Thus, the answer to the question is "yes," provided that the polymorphism lies close enough to the gene in question (the one that exerts an influence) so that it is rarely separated from the gene by recombination. When DNA polymorphisms are located close to a gene, but not within the gene itself, they are called markers for that gene.

2. What criterion did scientists use when assigning research subjects to Group 1 and Group 2? Why do you think the subjects were organized in this way? Would a random population make it easier or more difficult to identify potential genes involved in novelty seeking?

Students should notice that the average novelty-seeking score is much higher in Group 1 than in Group 2 (42.8 compared to 35.0). Moreover, there is no overlap in scores between the two groups. The lowest score in Group 1 is 41, and

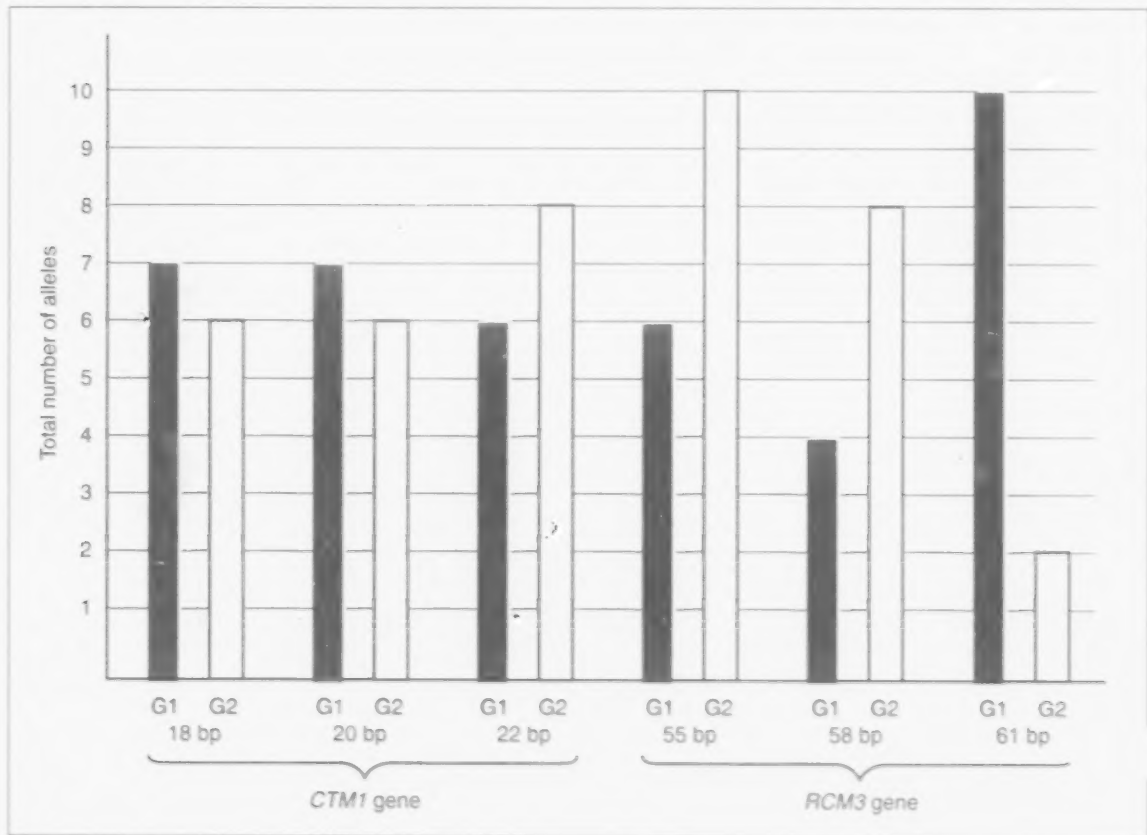


Figure T4.3 Completed histogram of allelic frequencies.

the highest score in Group 2 is 37. Thus, it appears that the groups were assigned according to high versus low novelty-seeking scores.

The subjects were organized in this way because comparing experimental populations at opposite ends of a distribution (remember that novelty seeking is continuously distributed) offers the best chance of revealing genes that might influence a behavior. In other words, if there are genes influencing novelty seeking, populations that are disparate for that trait should highlight the genetic differences. This is akin to searching for a genetic predisposition to disease by comparing DNA polymorphisms from affected persons with unaffected persons. (Note that failing to detect a difference does not rule out a genetic influence; the contribution of any single gene may simply be too small to detect. Likewise, a high correlation between a gene and a trait does not prove causation; other experiments must be done to prove that there is a functional or mechanistic relationship between the candidate gene and the phenotype.)

A random population would show a mix of novelty-seeking scores and no clear distinction between high scorers and low scorers. Likewise, even if genes were involved in the behavior, they would be distributed among many genes of little importance to novelty seeking. The distribution of alleles would be very broad and likely would hide candidate genes. In other words, potentially important alleles might not appear at high enough frequency to make their appearance noticeable. Thus, a random population would make it more difficult to distinguish genes that influence the behavior at either extreme.

3. What is the relationship between the RCM3 allele 61 and the novelty-seeking scores? Explain whether that relationship offers evidence that a particular gene might influence novelty-seeking behavior.

The frequency of RCM3 allele 61 is much higher in Group 1 than in Group 2 (10 compared to 2), which suggests that allele 61 may influence high novelty seeking. This correlation of allele 61 with high scores (even if statistically significant), however, does not prove that allele 61 causes

high novelty-seeking behavior. Correlation alone is never evidence of causation. (For more information on determining statistical significance, see the extension activity.)

4. What is the relationship between the RCM3 alleles 55 and 58 and the novelty-seeking scores? Explain whether those relationships offer evidence that genes might influence novelty-seeking behavior.

The frequency of RCM3 alleles 55 and 58 is higher in Group 2 than in Group 1 (10 compared to 6, and 8 compared to 4, respectively), which might suggest that the combination of the 55 and 58 alleles influences low novelty seeking. As stated earlier, this correlation, even if statistically significant (which cannot be determined by observation alone), does not prove that alleles 55 and 58 cause low novelty-seeking behavior. Nevertheless, the data are provocative because in the case of both high-score and low-score correlations, gene RCM3 is involved. Further experiments would be necessary to demonstrate a causative relationship.

5. Do the data provide reasons for caution as to the role that RCM3 allele 61 plays in influencing novelty-seeking behavior? Use specific examples from the data to defend your answer. What other factors might be important in novelty-seeking behavior?

Yes, caution is warranted, and the data do not support causative conclusions. There is ample evidence to support the involvement of factors other than the RCM3 allele 61: (1) Some subjects with high scores do not have allele 61 (subjects 1 and 7); (2) Some subjects with low scores do have allele 61 (subjects 17 and 19). Clearly, additional factors influence novelty-seeking behavior, but the data available do not allow us to determine whether those other factors are genetic or environmental. Both are possible and, in fact, likely.

(Observant students may notice that the two individuals who are homozygous for allele 61 [subjects 2 and 6] have the highest novelty-seeking scores [44 and 45, respectively], which suggests that two copies of this allele might increase the likelihood for scores that are high. Subjects 7

and 10 also score 44, however, and subject 7 has no copies of allele 61 whereas subject 10 has only one copy.)

6. **What is the relationship, if any, between the *CTM1* gene and novelty-seeking behavior?**

CTM1 does not appear to segregate with any apparent pattern relative to the novelty-seeking scores. That gene may represent simply an unimportant or trivial polymorphism in those subjects' genomes. On the other hand, if we had additional information about all of the subjects—for example, eye color, height, scores on anxiety tests, and measures of hand-eye coordination—we might discern associations between other traits and *CTM1*.

7. **Challenge: What additional studies might behavioral geneticists perform to test their hypothesis that *RCM3* allele 61 influences high novelty-seeking behavior?**

First, behavioral geneticists carefully apply statistical analysis to such studies to rule out the possibility that observed correlations between genetic markers and traits are due only to chance. Second, to validate their results, behavioral geneticists require corroborative evidence from several markers in different populations, and using different methods. For example, in this scenario, behavioral geneticists would select several additional markers that are all found in the same chromosome region near *RCM3*. If all of those additional markers also associated with high scores, but not low scores, the researchers would be more confident in making predictions that future, untested high scorers also would have a

higher likelihood of possessing the 61 allele.

This confidence would be strengthened further if markers to regions of other chromosomes (chosen randomly) did not segregate with high scores and if a test in a different population of individuals with high scores also showed association with allele 61 of *RCM3*. Of course, even in the face of this additional evidence, the existence of subjects with high scores and no allele 61, or of subjects with low scores and allele 61, would demonstrate that factors other than allele 61 also were critical to novelty seeking.

Finally, researchers could try to identify the actual function of the candidate gene by testing it in nonhuman animal models. For example, if geneticists found a homologous gene in rats or mice—a gene that had a sequence very similar or identical to *RCM3* in humans—they could manipulate the gene by mutation or deletion to explore the effects that those changes might have on the organisms' behavior. If the changes appeared to affect a behavior analogous to novelty seeking in humans, then scientists may indeed have discovered a causative relationship. Defining analogous behaviors in other animals, however, is difficult and controversial.

Extension: Chi-square calculation (optional)

In the extension activity, students can learn to do a chi-square analysis to test whether the differences observed in allele frequencies for the *RCM3* gene are significant in a formal statistical sense. See extension pages for more details.

Activity 4 Extension: Chi-Square Calculation

In the context of Activity 4, *Finding the Genes That Influence Novelty-Seeking Behavior*, the chi-square calculation is used to test whether allele frequencies between groups of high and low scorers reflect real differences between populations or just fluctuations due to chance. If you have never done a chi-square analysis or would like to understand the concept better, read the student pages carefully.

This activity is appropriate for students who have had a basic introduction to the concepts of probability and statistics. If students have not been exposed previously to these ideas, then the material in the student pages should be presented thoroughly before performing the chi-square calculations. Answers to the chi-square analysis for the RCM3 and CTM1 genes are provided below.

Table T4.1 Observed Allele Frequencies for the RCM3 Gene

Frequency	61 bp	58 bp	55 bp	Row Total
High	10	4	6	20
Low	2	8	10	20
Column Total	12	12	16	40

To calculate the expected frequencies, multiply the observed row total by the observed column total and divide by the total sample size as shown for the RCM3 gene.

Expected frequencies:

$$\begin{aligned} \text{allele 61/high} &= (20)(12) \div 40 = 6 \\ \text{allele 58/high} &= (20)(12) \div 40 = 6 \\ \text{allele 55/high} &= (20)(16) \div 40 = 8 \\ \text{allele 61/low} &= (20)(12) \div 40 = 6 \\ \text{allele 58/low} &= (20)(12) \div 40 = 6 \\ \text{allele 55/low} &= (20)(16) \div 40 = 8 \end{aligned}$$

Table T4.2 Expected Allele Frequencies for the RCM3 Gene

Frequency	61 bp	58 bp	55 bp	Row Total
High	6	6	8	20
Low	6	6	8	20
Column Total	12	12	16	40

The chi-square value χ^2 for the set of data is then calculated using the following formula:

$$\chi^2 = \sum (\text{observed number} - \text{expected number})^2 \div \text{expected number}$$

$$\begin{aligned} \chi^2 \text{ for 61/high} &= (10 - 6)^2 \div 6 = 4^2 \div 6 = 2.67 \\ \chi^2 \text{ for 58/high} &= (4 - 6)^2 \div 6 = -2^2 \div 6 = 0.67 \\ \chi^2 \text{ for 55/high} &= (6 - 8)^2 \div 8 = -2^2 \div 8 = 0.50 \\ \chi^2 \text{ for 61/low} &= (2 - 6)^2 \div 6 = -4^2 \div 6 = 2.67 \\ \chi^2 \text{ for 58/low} &= (8 - 6)^2 \div 6 = 2^2 \div 6 = 0.67 \\ \chi^2 \text{ for 55/low} &= (10 - 8)^2 \div 8 = 2^2 \div 8 = 0.50 \end{aligned}$$

$$\text{Total } \chi^2 \text{ value} = 7.68$$

The calculated chi-square value is next compared to others in a table of critical values to determine if it is significant. For our analysis, the degrees of freedom are calculated according to $(r - 1)(c - 1)$, where r is the number of rows in the table and c is the number of columns in the table. For the RCM3 example, the degrees of freedom are $(2 - 1)(3 - 1) = 2$.

The chi-square value calculated for RCM3 is 7.68. The critical values of chi square for 2 degrees of freedom are 5.99 for $p = 0.05$ and 9.21 for $p = 0.01$. Therefore, the deviation from chance association between allele type and group for RCM3 is significant at $p < 0.05$. In other words, the association between novelty-seeking scores and the allele types for RCM3 is stronger than we would expect than if it were just a chance association.

Table T4.3 Excerpt from a Chi-Square Table

Degrees of Freedom	p-values			
	0.10	0.05	0.01	0.005
1	2.71	3.84	6.63	7.88
2	4.61	5.99	9.21	10.60
3	6.25	7.81	11.34	12.84
4	7.78	9.49	13.28	14.86

Table T4.4 Observed Allele Frequencies for the CTM1 Gene

Frequency	22 bp	20 bp	18 bp	Row Total
High	6	7	7	20
Low	8	6	6	20
Column Total	14	13	13	40

Expected frequencies:

$$\begin{aligned} \text{allele 22/high} &= (20)(14) \div 40 = 7.0 \\ \text{allele 20/high} &= (20)(13) \div 40 = 6.5 \\ \text{allele 18/high} &= (20)(13) \div 40 = 6.5 \\ \text{allele 22/low} &= (20)(14) \div 40 = 7.0 \\ \text{allele 20/low} &= (20)(13) \div 40 = 6.5 \\ \text{allele 18/low} &= (20)(13) \div 40 = 6.5 \end{aligned}$$

Table T4.5 Expected Allele Frequencies for the CTM1 Gene

Frequency	22 bp	20 bp	18 bp	Row Total
High	7	6.5	6.5	20
Low	7	6.5	6.5	20
Column Total	14	13	13	40

The chi-square value is calculated from these observed and expected cell frequencies in the same manner as for RCM3:

$$\chi^2 = \sum (\text{observed number} - \text{expected number})^2 \div \text{expected number}$$

$$\begin{aligned} \chi^2 \text{ for 22/high} &= (6 - 7)^2 \div 7 = (-1)^2 \div 7 = 1 \div 7 = 0.14 \\ \chi^2 \text{ for 20/high} &= (7 - 6.5)^2 \div 6.5 = 0.04 \\ \chi^2 \text{ for 18/high} &= (7 - 6.5)^2 \div 6.5 = 0.04 \\ \chi^2 \text{ for 22/low} &= (8 - 7)^2 \div 7 = 0.14 \\ \chi^2 \text{ for 20/low} &= (6 - 6.5)^2 \div 6.5 = 0.04 \\ \chi^2 \text{ for 18/low} &= (6 - 6.5)^2 \div 6.5 = 0.04 \end{aligned}$$

$$\text{Total } \chi^2 \text{ value} = 0.44$$

Again using the chi-square table, what does your calculated value for chi square tell you about the association between CTM1 allele types and novelty seeking?

Using the chi-square table at 2 degrees of freedom, the chi-square value of 0.44 is much lower than the value associated with $p = 0.05$. Therefore, there is no evidence of an association between novelty-seeking and any of the CTM1 allele types.

Activity 5

Paula's Law

Overview

This activity serves as a conclusion to the module by asking students to take policy positions on the impact of hypothetical legislation that would restrict the purchase of beverage alcohol. The purpose of this activity is to have the students appreciate the challenges involved in using scientific information about the variability of human behavior to set policy choices. The policy situation that they will explore involves genetic predisposition to alcohol abuse.

Students first encounter a hypothetical young adult who reflects on her own history of alcohol abuse. They then evaluate a proposed law that seeks to minimize the social costs associated with alcohol abuse and dependency. Once the basic issues are understood, students physically move to different parts of the room to register their opinions on the proposed legislation. A discussion allows students to change their opinions based on the reasoning of their peers. Finally, students use the information they have learned in the module to write a scientific evaluation of the law at the center of this activity.

Major concepts

- Knowledge arising from the study of behavioral genetics will have implications for the formulation of social policy.
- The impact of behavioral genetics likely will increase in the future.
- Individual human behavior cannot be determined from the results of population studies.

Estimated time

50–75 minutes

Learning outcomes

In this activity, the students will

1. understand how to analyze data from behavioral genetics in the context of a proposed social policy;
2. recognize the scientifically appropriate and inappropriate uses of data from behavioral genetics in making public policy;
3. advocate a position on proposed legislation that would regulate the sale and distribution of alcoholic beverages; and
4. evaluate the scientific claims in the proposed legislation and present them, using information from the entire module, in written form.

Materials (per team of two)

- 15 copies of Copymaster 5.1, *Reasons in Favor of and Against Paula's Law*
- 15 copies of Copymaster 5.2, *Applegate Genotype Results*

Process and procedures

Introduce this activity by asking students to raise their hands if they think that alcohol is a problem in contemporary society. Ask those who raise their hands what some of the problems are. At this point, the goal is to get students thinking about the role of alcohol in society. Ask whether they think the purchase of alcoholic beverages should be more—or less—restricted than it is currently. Encourage any answer to be supported by credible reasoning, not knee-jerk responses.

Explain that this activity will build on the information from the previous activities about research into behavioral genetics, including continuous variability of complex traits, the relative contributions of genes and the environment to behavior, and methods of evaluating genetic risk. Some of the methods for genotyping simulated in Activity 4 could actually be used for obtaining the genotypes discussed in this activity.

Step 1. Ask students to read the excerpt from Paula's diary dated March 2, 2001. Take just a brief moment to clarify what Paula is saying in her diary. That can be accomplished by asking the class to relate the sequence of events Paula outlines from that first drink in eighth grade up to the day she wrote the entry.

Step 2. Ask students to read *Proposing a Change*. Emphasize that the four genes influencing alcohol dependence have not been identified by researchers. The scientific information used to support Paula's Law in this activity is hypothetical.

Step 3. Have students form teams of two and read *Senator Applegate's Speech before the United States Senate* and the *Press Release on Paula's Law* carefully with an eye toward identifying reasons for and against the proposed legislation. Most of the policy information is contained in the senator's speech; most of the scientific information is found in the press release. Although students may begin by dividing responsibility for examining these information sheets, it is likely that they will need to consult each other when completing the chart, *Reasons in Favor of and Against Paula's Law*. Caution students to hold off on judging this proposed law until they have more facts. You may want to discuss with students, if the issue arises, the reliability of the information in the press release. For the purposes of this activity, be sure that students understand that the information presented by Senator Applegate is correct and reflects both current and expected research in behavioral genetics. If you discern a need to clarify some of the information in the press release, help students identify statements that support the following major concepts.

- a. Both genetic and environmental factors contribute to risk for alcohol dependence. For example, the four loci contribute to only 55 percent of the total risk of alcoholism; although other loci may be discovered in the future, the remaining 45 percent of risk is likely to be environmental.

- b. The genotypes described in the press release actually have predictive validity, but this validity is limited. That is, some people with the genetic risk factors will not develop alcohol dependence and some people without these risk factors will develop alcohol dependence. Students will see that clearly after Step 4, but the general concept should be familiar from the preceding activities.

- c. Although genetic data are often discussed as if these data were *categorically* different in predictive value from other kinds of data, that is not the case. For example, demographic data on teen driving taken from police records has limited value in predicting how any individual teen will drive, but those data are used nonetheless in setting insurance rates for individuals. Moreover, for the phenotype of alcohol dependence, other data can be collected that undoubtedly would have better predictive validity than the genetic data modeled here. For example, history of alcohol abuse has greater predictive validity for future dependence than any set of genetic markers likely to be discovered.

Table T5.1 lists possible reasons to support and oppose the legislation. Ask students to justify each reason. Emphasize the role of evidence in supporting reasons. The underlying research into behavioral genetics should figure prominently in the students' reasoning, as well as the plausibility of the genetic research in light of the dynamic nature of scientific information, especially novel research findings such as those in behavioral genetics.

Step 4. To help students further understand the science contained in the senator's press release and how that relates to his own family, use Copymaster 5.2, *Applegate Genotype Results* and Figure 5.1, *Applegate Family Pedigree and Risk Table*. Instruct the students to use the *Applegate Genotype Results* to determine the genotypes for Paula's parents, brother, and sister, and write them in the appropriate spaces in the family pedigree. Next, have the students total the number of homozygous high-risk loci for each family member and write them in the risk table.

Copymaster 5.2, *Applegate Genotype Results*, shows how a DNA analysis examining these four loci for the five individual Applegate family members might

Table T5.1 Reasons for and Against Legislation

In Favor of Legislation	Against Legislation
• saves lives/addresses a serious problem • situation calls for urgent attention • is primarily a preventive policy • keeps alcohol out of hands of those most likely to use irresponsibly • is nonintrusive for most people • could reduce insurance, medical, employment costs • seeks to prevent an irreversible harm • 13% of population is at risk and alcohol abuse is very costly • has potential far-reaching benefits in preventing violence, suicide, employers' costs (lost time and productivity), traffic fatalities, and injury • regulates purchase, not possession of alcohol • keeps alcohol consumption legal, if you don't have the four high-risk genotypes	• is intrusive by taking bodily fluid (cheek cell sample/ invasion of privacy) • government is not reliable in carrying out such functions • leaves DNA in the hands of the government, which could use it to test for other things • benefits achieved at cost of restricting access to alcohol for many people unnecessarily • there are better ways to achieve the goal using existing public policies such as DWI convictions • will raise prices of beverage alcohol for everyone • test could have unanticipated consequences such as detection of nonpaternity and nonmaternity • would promote black market for alcohol or for the Alcohol Freedom Card • it's none of the government's business if I want to drink myself to death • lab errors will result in groundless discrimination or failure to protect at-risk individuals • may encourage use of other drugs, including illegal drugs • there are better ways to prevent drunk driving, for example, putting Breathalyzer ignition interlocks in all cars • has very imperfect genetic predictability, thus punishing some innocent people • punishes people according to a genetic test, not behavior

appear. These data can be used to illustrate the results of gel electrophoresis, a process that was studied in Activity 4, and that might be performed in the proposed government laboratory (in conjunction with PCR) to analyze the cheek cell samples. The data represented allow students to complete the pedigree table.

4a. What evidence from behavioral genetics is included or implied in Senator Applegate's legislation and press release? Is the genetic evidence fundamentally more valuable than nongenetic evidence, such as the number of driving-while-intoxicated (DWI) citations?

Recall at this point that the genetic loci discussed in the senator's speech account for just 55 percent of the risk for alcohol dependence (see Figure 5.2 in the *Press Release on Paula's Law*.) Students should point out that there must be other factors (probably both genetic and environmental) accounting for the remainder of the risk.

In any event, it should be quite clear that the senator regards the genetic data as categorically more valuable than the environmental data in predicting future risk. Basically, this is an error on his part. He could achieve his goal of reducing the costs to society of alcohol dependence in other ways, for example, by using the history of alcohol abuse evaluated by an interview or other means to determine who gets an Alcohol Freedom Card, or by advocating the lifetime revocation of driving privileges after a single DWI incident. But, there are weaknesses to that approach also; it only works after the person has exhibited dangerous behavior. The genetic screening proposed by the senator would prevent such behavior, in some cases, before it has been manifested by the subject in any form. The two approaches identify an intersecting, but not completely overlapping, set of individuals at risk for alcohol-abuse-related behaviors. The second approach (nongenetic) has the advantage of not intruding on the lives of people who never would exhibit risk-related behaviors.



Figure T5.1 The Applegate family pedigree and risk table combined with the *Applegate Genotype Results* allow students to determine the genotypes for each family member. High-risk alleles are indicated by lowercase letters. All four high-risk alleles are assumed to show recessive inheritance and, therefore, only show their effect in the homozygous state (shown as a pair of lowercase letters). This pedigree can be used to trace the inheritance of the alleles through the family and to illustrate the relationship between genotype and alcohol dependence. Note that Paula's brother, Bob, has all four high-risk loci and is not an alcoholic and that her father, the senator, has only three high-risk loci and yet is an alcoholic.

4b. Where are the influences of genes acknowledged?

The genetic influence on alcoholism is acknowledged through the collection, analysis, and storing of genotype data.

4c. Where are the influences of environment acknowledged?

The environmental influence on alcoholism is acknowledged through the prohibition of further alcohol purchases for individuals with a record of excessive alcohol purchase. This prohibition is applied regardless of the individual's genotype.

Step 5. The important observations from the *Applegate Genotype Results* and the Applegate family pedigree and risk table are that Paula's brother, Bob,

is homozygous at four high-risk loci (as is Paula), yet he is not alcoholic. That information should cause students to temper their enthusiasm for the senator's bill. Moreover, the senator himself has only three high-risk loci, but is an alcoholic nonetheless.

Step 6. This step forces the students to focus on the most important reasons for and against Paula's Law in preparation for determining their own position on the legislation. Encourage students to return to the various sources of information in the senator's speech, press release, the *Applegate Genotype Results*, the Applegate family pedigree and risk table, as well as what they have learned in the module.

Steps 7–8. This step requires that students get out of their seats and move to different locations in the classroom (see Figure T5.2). Identify one corner of the room as the location of "Strongly supports this legislation" and the opposite corner as "Strongly opposes

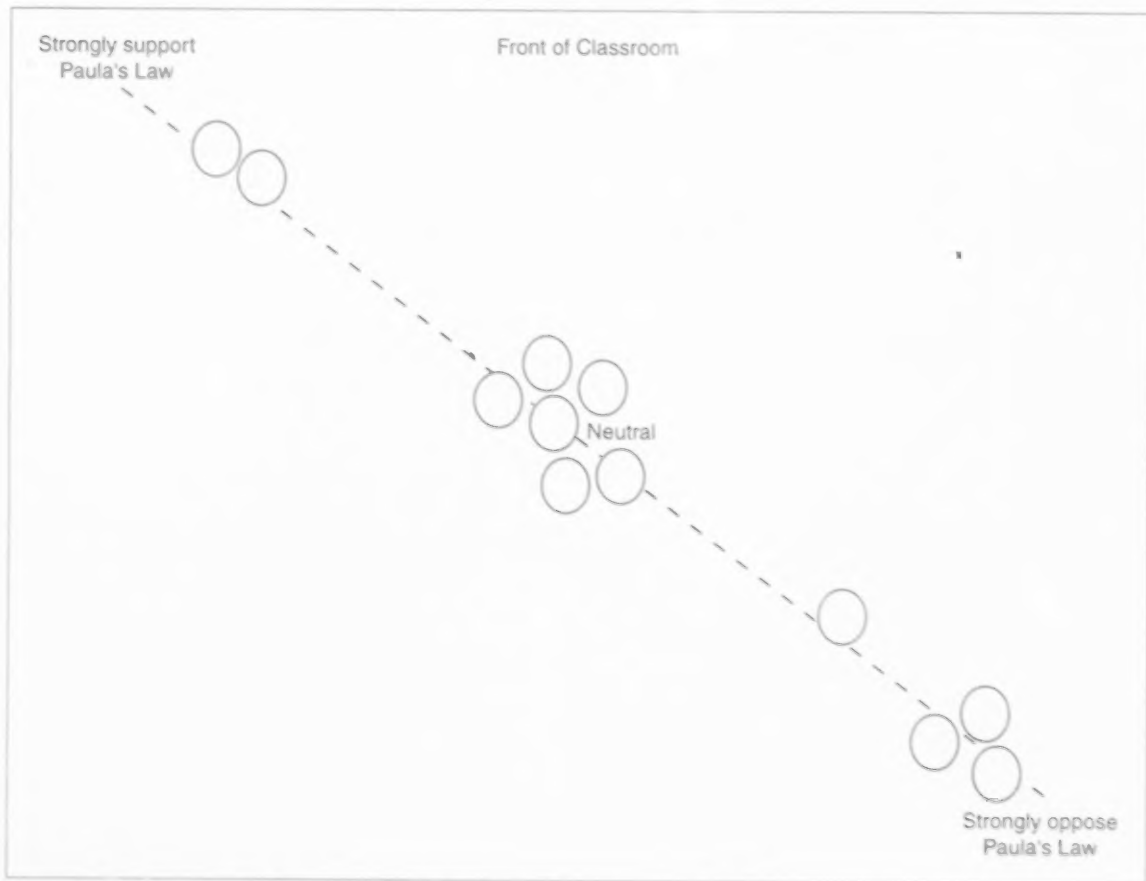


Figure T5.2 Top view of students arranging themselves in classroom according to opinion.

this legislation." The middle of the room is the neutral position. Ask the students to align themselves along this continuum by locating themselves at the point that best represents their opinion on Senator Applegate's legislation or a position they would like to advocate. Be sure students understand that taking a "devil's advocate" position is both appropriate and important in public policy discussions.

Several outcomes are possible. You might get a relatively wide distribution. In that case, ask students to articulate why they placed themselves where they did in relation to the extremes. Ask students who are close to each other why each is closer or farther from the extreme. The primary goal of this strategy is for students to compel each other with their reasoning and logic and to hear each other so that they might see the need to alter their relative location along the continuum. Encourage these movements and explanations for changing location.

If students clump in one or two locations, push each of them to articulate the reasons for their positions and what changes in the proposed legislation might help alter an individual's location. If all students cluster at one extreme, ask for volunteers or assign students to move elsewhere and argue a different position on Paula's Law. Because students are up and out of their seats, set as a clear norm that they *must* listen to each other and that *only one person speaks at a time*. When orchestrated correctly, there is a fluidity that mirrors the changing positions on complex issues in society at large and that often accompanies the public-policy adoption process.

As you listen to the students' reasons and reasoning, you might want to challenge them using some of the language of public policy analysis. Criteria that are used include effectiveness and urgency (see *Teacher Background*).

Effectiveness means that scientifically valid or technologically practical means are available, or could be created, to prevent, reduce, or avoid risk of serious, far-reaching, and irreversible harm. The public policy also must be enforceable—resources must be available to finance the policy, penalties for failure to comply must be reasonable and able to be effectively imposed, and a majority of the population must be expected to comply. For example, is provision #1 of Paula's Law (providing a cheek cell sample) likely to result in high levels of noncompliance?

Urgency means that there is immediate risk of serious, far-reaching, and irreversible harm if the legislation is enacted or the law is not changed. For example, is the need to prevent the individual and social consequences of alcohol abuse, such as automobile wrecks, a serious matter?

Step 9. Once students vote on the legislation, ask them to explain which argument or arguments were most persuasive. If the vote ends in a tie, you might cast a tie-breaking vote. The reality of a democracy is that the minority view must submit to the will of the majority, at least within reasonable ethical bounds.

Students might want to change Senator Applegate's legislation to make it more acceptable. As time allows, this is a worthwhile extension. You may want to involve a civics teacher in this part of the activity, with the intention of modeling procedures used by the Senate in amending and voting on legislation.

Analysis questions

1. In what ways does Senator Applegate's proposed legislation appropriately use information gained from research into behavioral genetics? In what ways is the information used inappropriately?

Appropriate:

- Increasing number of high-risk loci increases the likelihood of alcoholism.
- From the histogram, only with four high-risk loci does the population risk exceed 50 percent. The senator's bill requires all four high-risk loci to be present before restricting alcohol purchase.

Inappropriate:

- The senator seems to confuse genetic predisposition with actual phenotype. Obviously, some individuals with all four high-risk alleles avoid becoming alcoholics.
- The senator's bill does not allow for choice because it examines only genes, not environmental factors or personal history.

2. How might things have been different if Paula had grown up in a home or community where use of alcohol was prohibited and access to alcohol was impossible? In such a case, would Paula's genetic background matter? Why or why not?

In this case, her behavior would not be influenced by her genetic background because she would not be exposed to alcohol and, therefore, would not develop alcohol dependence or abuse, so long as these environmental conditions continued. Despite the possibility that her genotype included the four susceptibility genes, her phenotype would not include alcohol dependence or abuse. This does not mean necessarily that she would not have died for some other reason.

3. What other actions could we take, besides using the findings from behavioral genetics, to minimize the problems associated with alcohol dependence and abuse?

Answers will vary, but might include reference to enacting stricter laws related to alcohol-related crimes and promoting stricter enforcement of current laws, continuing efforts at designated driver programs, promoting nonalcoholic social events for youth, providing additional counseling opportunities and support for individuals who manifest behaviors related to alcohol dependence, requiring Breathalyzer ignition interlocks on all vehicles, or a mandatory interview to determine history of alcohol use.

4. How would you have responded if Senator Applegate had stated that a single gene had been discovered that accounts for all of the risk of alcohol dependence? Explain.

Make sure that students refer to and use the discussion from Activity 1 about the hypothetical discovery of a single gene accounting for differences in intelligence. They should conclude that Paula's Law would be based on bad science.

Students should understand that alcohol dependence, like intelligence and novelty seeking, is a complex trait. Coincidentally, the relative contributions of genetic and environmental factors to intelligence and alcohol dependence are similar.

Pulling it all together

To conclude the activity and the module, have the students pretend that the editor of your school newspaper has asked them to write a short scientific evaluation of Senator Applegate's proposed legislation. Their articles should serve as scientific critiques of the proposed policy and should use references to information and concepts from at least three of the activities in this module. Points in their critiques should include the following:

- Alcohol abuse is a multifactorial trait, having both genetic and environmental components.
- Twin studies have demonstrated a significant genetic contribution to alcohol dependence.
- Gene-association studies have identified four loci that correlate with high risk for alcohol abuse (hypothetically, for this activity).
- These four genes together account for only 55 percent of the risk for alcohol dependence.
- Individuals having all four high-risk alleles may not abuse alcohol.
- Individuals having fewer than four high-risk alleles still may become alcoholics.

- Students may hold different opinions about Paula's Law, but their views must be consistent with the scientific findings listed above. Assess the students on their basic writing skills, the degree to which they refer to and explain principles of behavioral genetics from the module, and the clarity of their ideas.

Copymasters

Copymaster 1.1
Late Breaking News: Gene for Intelligence Discovered

The Gotham Daily Herald

Special Edition

January 1, 2000

Late Breaking News: Gene for Intelligence Discovered!



Dr. I.Q. Cerebrum announces the discovery of the intelligence gene.

BOSTON. Yesterday, scientists made the startling announcement that they have located a single gene that accounts for human intelligence. Almost unbelievably, this one gene appears to determine the degree of intelligence that any given individual will have in his or her lifetime. The intelligence gene has only two different alleles. Researchers are testing the hypothesis that the intelligence trait shows a codominant inheritance pattern.

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Copymaster 2.1
Human Variation Worksheet—Female

In this model, six genes, each with two alleles, influence height, and various environmental factors influence height depending on the stage of development. Your teacher will provide the numerical values of the various colored beads for both genetic and environmental effects *after* you have completed the drawing the beads.

Part I: Modeling Genetic Influence

Gene	Bead Color	Effect in cm
1		
2		
3		
4		
5		
6		

Genetic influence _____

Part II: Modeling Environmental Influence

Factor	Bead Color	Effect in cm
Prenatal		
Childhood		
Adolescence		

Environmental influence _____

Females' starting height: 165 cm

Final height = starting height + genetic influence + environmental influence

Final height = ____ + ____ + ____ = ____ cm

Copymaster 2.2
Human Variation Worksheet—Male

In this model, six genes, each with two alleles, influence height, and various environmental factors influence height depending on the stage of development. Your teacher will provide the numerical values of the various colored beads for both genetic and environmental effects *after* you have completed drawing the beads.

Part I: Modeling Genetic Influence

Gene	Bead Color	Effect in cm
1		
2		
3		
4		
5		
6		

Genetic influence _____

Part II: Modeling Environmental Influence

Factor	Bead Color	Effect in cm
Prenatal		
Childhood		
Adolescence		

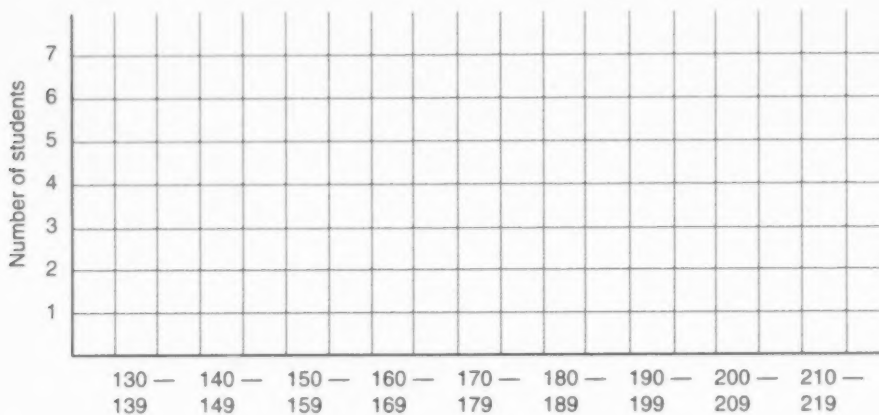
Environmental influence _____

Males' starting height: 175 cm

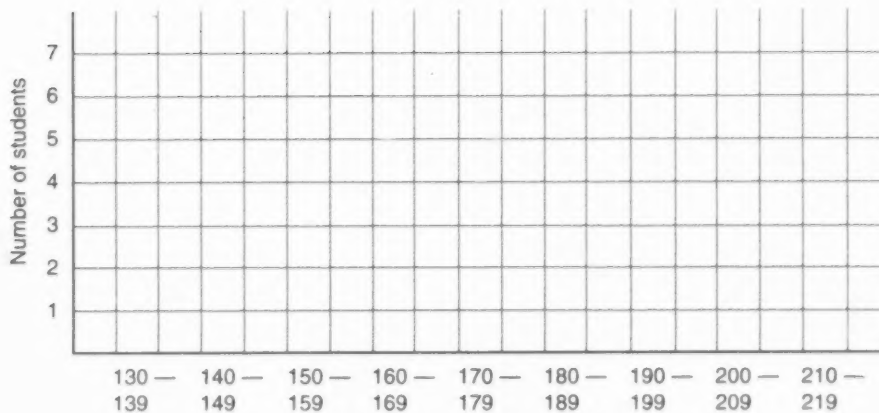
Final height = starting height + genetic influence + environmental influence

Final height = ____ + ____ + ____ = ____ cm

Copymaster 2.3
Histogram Template for Heights



Population of females
Height in centimeters - influenced by genetic and environmental factors



Population of males
Height in centimeters - influenced by genetic and environmental factors

Copymaster 2.4
Modeling Genetic and Environmental Influences

Part I: Modeling Genetic Influence

For each of the six genes:

red allele +2 cm

white allele -2 cm

Part II: Modeling Environmental Influence

Prenatal

orange factor -4 cm Mother smoked 1½ packs of cigarettes a day and was a heavy drinker of alcoholic beverages.

yellow factor 0 cm Mother was on a very low protein diet and sought no prenatal care.

green factor +2 cm Family income below poverty level, but the family did its best to provide the mother with adequate nutrition and prenatal care; no maternal smoking, no alcohol intake.

blue factor +4 cm Mother had normal nutrition, no alcohol intake or smoking, and good prenatal care.

Childhood

orange factor -4 cm Chronic kidney infection leading to renal failure and transplant of a kidney at age ten years.

yellow factor -2 cm Family income below poverty level, inadequate nutrition.

green or blue factor 0 cm No environmental factors sufficient to affect adult height for green or blue.

Adolescence

orange factor -2 cm Severe nutritional deprivation; for example, diet consisting of mostly junk foods; anorexia and/or bulimia.

yellow, green, or blue factor 0 cm Free of chronic disease, adequate nutrition.

Copymaster 3.1 Novelty-Seeking Survey

Do not write on this survey.

Keep a tally on a separate piece of paper of how many items you respond "yes" to.

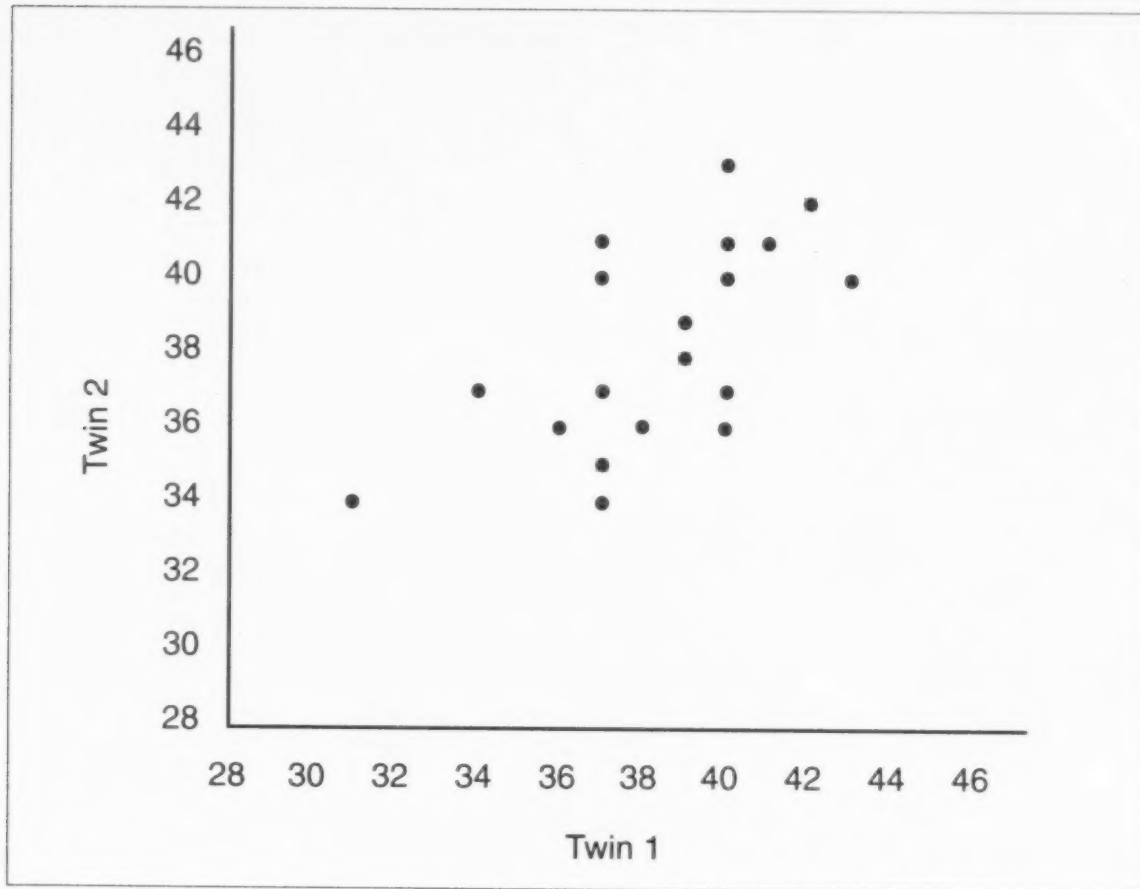
Which of the following have you done or would you be willing to do?

1. jump from a 20-foot cliff into 10 feet of water
2. drive a car 100 mph
3. travel alone to a new city
4. ride a motorcycle without a helmet
5. hitchhike a ride from a stranger
6. play a sport you've never tried with strangers
7. pierce a body part other than your ear
8. dye your hair blue
9. go up in the space shuttle
10. sleep out overnight, alone in a forest
11. go up in a hot air balloon
12. take a trip in a submarine
13. sky dive
14. enter a burning building to rescue a cat or dog
15. scuba dive in shark-infested waters
16. crawl in a cave without a flashlight
17. hit a stranger in an argument
18. go for a ride in a small plane
19. take care of a beehive (wearing a bee suit)
20. ride a horse
21. target shoot with a handgun
22. accelerate to make it through a yellow traffic light
23. drink something blue
24. volunteer to give a class report first
25. travel to a non-English-speaking country
26. ride without a seatbelt in a car going more than 75 mph
27. participate in underage drinking
28. let a friend who was drunk drive you home
29. date a person of an ethnicity other than your own
30. eat raw fish (sushi)
31. support an unpopular viewpoint or person in front of your friends
32. pet a lion or tiger
33. hold a nonpoisonous snake
34. poke a rattlesnake with a stick
35. white-water raft
36. go over Niagara Falls in a barrel
37. climb a mountain
38. rappel (slide down ropes to descend a cliff)
39. drink water directly from a stream
40. eat something if you didn't know what it was
41. eat your taco if it fell on the restaurant floor

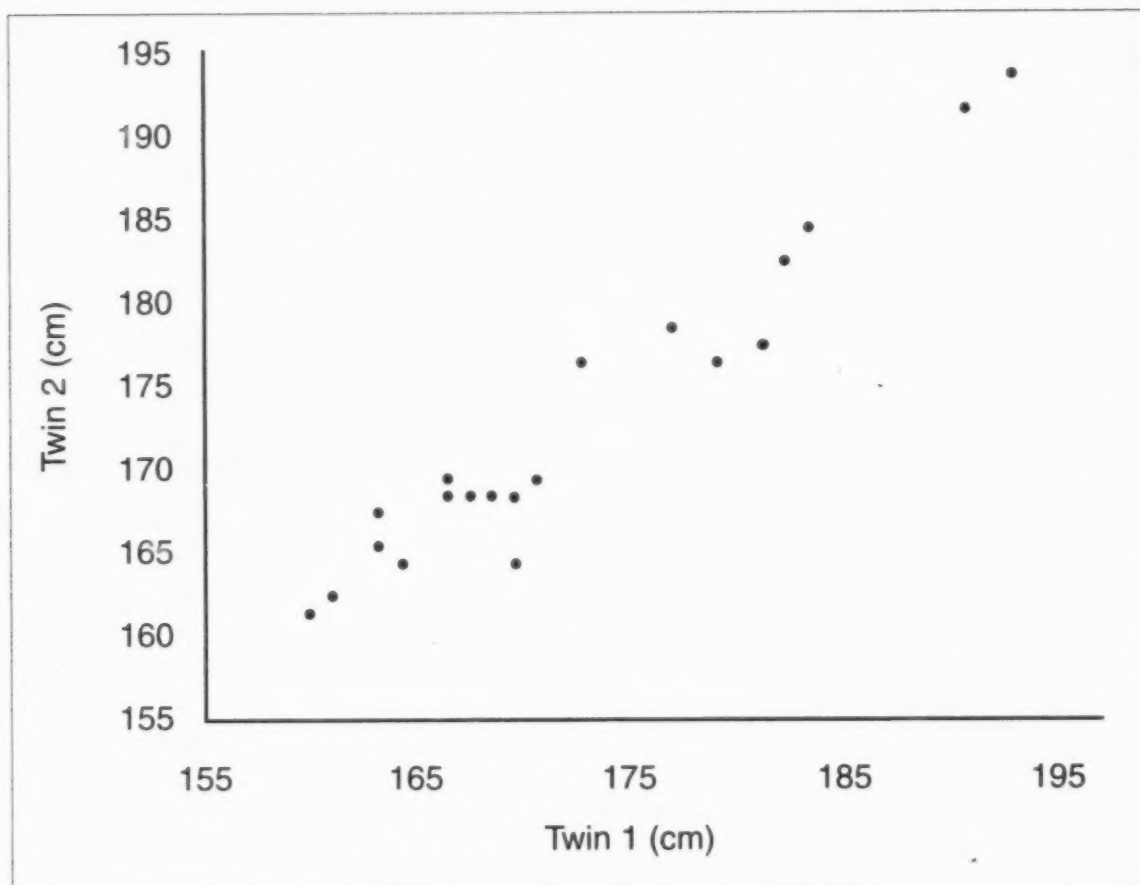
Copymaster 3.1 (continued)
Novelty-Seeking Survey

42. sit on a public toilet seat without wiping it off
43. sing in front of an audience
44. donate blood
45. wear your older brother's shirt if you knew he didn't want you to
46. cross the street without looking
47. ride the subway after midnight in New York City
48. downhill ski
49. go out on a blind date
50. walk home alone at night in a big city
51. wear more than six articles of jewelry
52. get a tattoo on a visible part of your body
53. bungee jump
54. work in a basement with lots of spiders
55. ride on the hood of a car
56. peaceably protest an apparent injustice
57. donate a kidney to an ailing relative
58. be first to walk across a frozen pond
59. take the final shot that will win or lose a basketball game
60. ask a girl/boy for a date
61. shoot off fireworks
62. participate in a human rights demonstration
63. take the first ride on a new roller coaster
64. ride with no hands on a roller coaster
65. go to a horror movie

Copymaster 3.2
Scatterplot of Novelty-Seeking Score Data for Identical Twins



Copymaster 3.3
Scatterplot of Height for Identical Twins

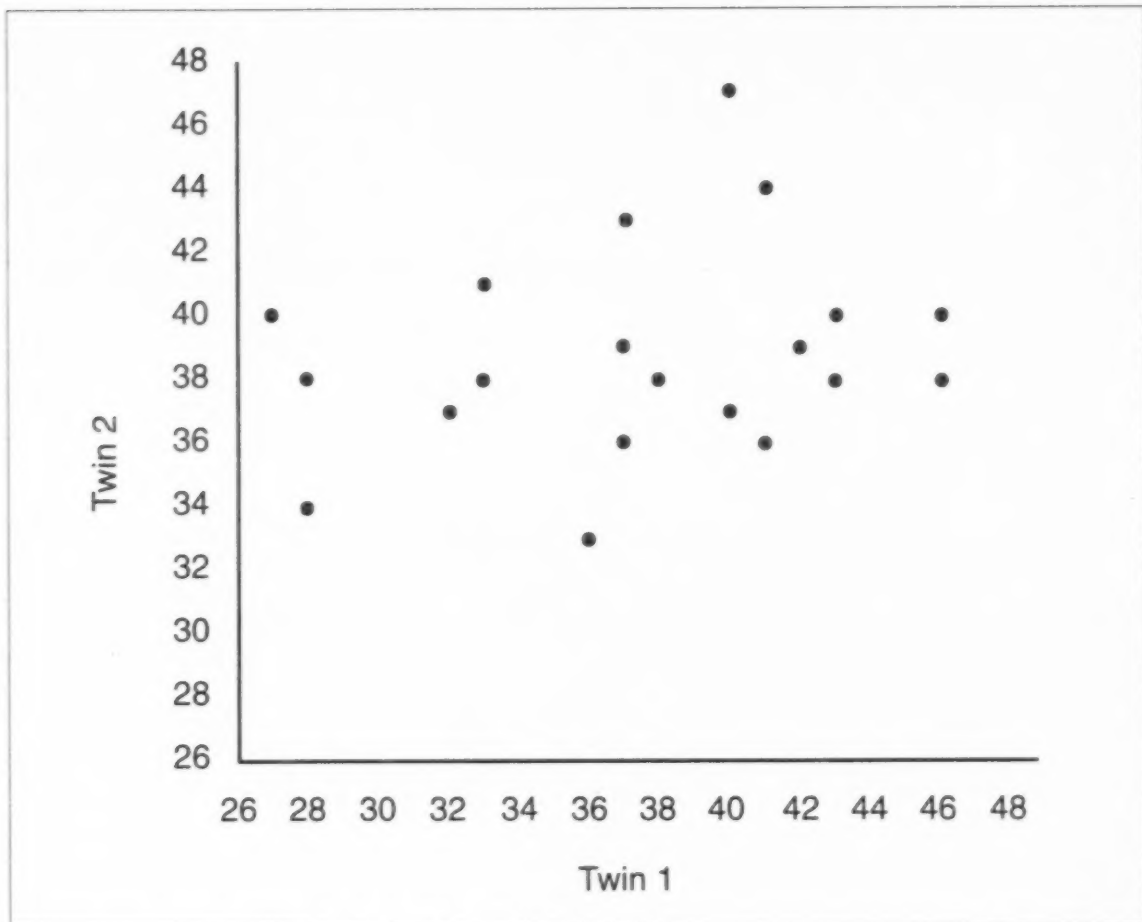


Copymaster 3.4
Novelty-Seeking Score Data for Fraternal Twins

The results of the novelty-seeking tests for fraternal (nonidentical) twins are shown below.

Twin Pair	Novelty-Seeking Score for Twin 1	Novelty-Seeking Score for Twin 2
A	40	37
B	41	36
C	43	40
D	32	37
E	46	40
F	27	40
G	42	39
H	33	38
I	37	43
J	28	38
K	43	38
L	38	38
M	33	41
N	36	33
O	41	44
P	37	39
Q	40	47
R	37	36
S	46	38
T	28	34

Copymaster 3.5
Scatterplot of Novelty-Seeking Score Data for Fraternal Twins



Copymaster 4.1
Group 1A Research Subjects:
Genotypes and High Novelty-Seeking Scores

Research Subject 1 - Novelty-Seeking Score = 42

CTM1 Gene, Allele A: AGGCTCACACACACATTGGC
CTM1 Gene, Allele B: AGGCTCACACACACATTGGC

RCM3 Gene, Allele A: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTCCTTGAAATCGGACGTACC
RCM3 Gene, Allele B: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTCCTTGAAATCGGACGTACC

Research Subject 2 - Novelty-Seeking Score = 44

CTM1 Gene, Allele A: AGGCTCACACACACACATTGGC
CTM1 Gene, Allele B: AGGCTCACACACACATTGGC

RCM3 Gene, Allele A: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTAGTCCTTGAAATCGGACGTACC
RCM3 Gene, Allele B: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTAGTCCTTGAAATCGGACGTACC

Research Subject 3 - Novelty-Seeking Score = 43

CTM1 Gene, Allele A: AGGCTCACACACATTGGC
CTM1 Gene, Allele B: AGGCTCACACACATTGGC

RCM3 Gene, Allele A: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTAGTCCTTGAAATCGGACGTACC
RCM3 Gene, Allele B: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTAGTCCTTGAAATCGGACGTACC

Research Subject 4 - Novelty-Seeking Score = 42

CTM1 Gene, Allele A: AGGCTCACACACACATTGGC
CTM1 Gene, Allele B: AGGCTCACACACATTGGC

RCM3 Gene, Allele A: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTAGTCCTTGAAATCGGACGTACC
RCM3 Gene, Allele B: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTCCTTGAAATCGGACGTACC

Research Subject 5 - Novelty-Seeking Score = 41

CTM1 Gene, Allele A: AGGCTCACACACACACATTGGC
CTM1 Gene, Allele B: AGGCTCACACACACACATTGGC

RCM3 Gene, Allele A: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTAGTCCTTGAAATCGGACGTACC
RCM3 Gene, Allele B: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTCCTTGAAATCGGACGTACC

Copymaster 4.2
Group 1B Research Subjects:
Genotypes and High Novelty-Seeking Scores

Research Subject 6 - Novelty-Seeking Score = 45

CTM1 Gene, Allele A: AGGCTCACACACACATTGGC
 CTM1 Gene, Allele B: AGGCTCACACACATTGGC

RCM3 Gene, Allele A: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTAGTCCTTGAAATCGGACGTACC
 RCM3 Gene, Allele B: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTAGTCCTTGAAATCGGACGTACC

Research Subject 7 - Novelty-Seeking Score = 44

CTM1 Gene, Allele A: AGGCTCACACACACATTGGC
 CTM1 Gene, Allele B: AGGCTCACACACATTGGC

RCM3 Gene, Allele A: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTCCTTGAAATCGGACGTACC
 RCM3 Gene, Allele B: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTCCTTGAAATCGGACGTACC

Research Subject 8 - Novelty-Seeking Score = 42

CTM1 Gene, Allele A: AGGCTCACACACACATTGGC
 CTM1 Gene, Allele B: AGGCTCACACACATTGGC

RCM3 Gene, Allele A: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTAGTCCTTGAAATCGGACGTACC
 RCM3 Gene, Allele B: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTCCTTGAAATCGGACGTACC

Research Subject 9 - Novelty-Seeking Score = 41

CTM1 Gene, Allele A: AGGCTCACACACATTGGC
 CTM1 Gene, Allele B: AGGCTCACACACATTGGC

RCM3 Gene, Allele A: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTAGTCCTTGAAATCGGACGTACC
 RCM3 Gene, Allele B: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTCCTTGAAATCGGACGTACC

Research Subject 10 - Novelty-Seeking Score = 44

CTM1 Gene, Allele A: AGGCTCACACACACATTGGC
 CTM1 Gene, Allele B: AGGCTCACACACATTGGC

RCM3 Gene, Allele A: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTAGTCCTTGAAATCGGACGTACC
 RCM3 Gene, Allele B: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTCCTTGAAATCGGACGTACC

Copymaster 4.3
Group 2A Research Subjects:
Genotypes and Low Novelty-Seeking Scores

Research Subject 11 - Novelty-Seeking Score = 33

CTM1 Gene, Allele A: AGGCTCACACACACATTGGC

CTM1 Gene, Allele B: AGGCTCACACACATTGGC

RCM3 Gene, Allele A: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTCCTTGAAATCGGACGTACC

RCM3 Gene, Allele B: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTCCTTGAAATCGGACGTACC

Research Subject 12 - Novelty-Seeking Score = 35

CTM1 Gene, Allele A: AGGCTCACACACACATTGGC

CTM1 Gene, Allele B: AGGCTCACACACATTGGC

RCM3 Gene, Allele A: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTCCTTGAAATCGGACGTACC

RCM3 Gene, Allele B: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTCCTTGAAATCGGACGTACC

Research Subject 13 - Novelty-Seeking Score = 34

CTM1 Gene, Allele A: AGGCTCACACACACATTGGC

CTM1 Gene, Allele B: AGGCTCACACACATTGGC

RCM3 Gene, Allele A: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTCCTTGAAATCGGACGTACC

RCM3 Gene, Allele B: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTCCTTGAAATCGGACGTACC

Research Subject 14 - Novelty-Seeking Score = 36

CTM1 Gene, Allele A: AGGCTCACACACACATTGGC

CTM1 Gene, Allele B: AGGCTCACACACATTGGC

RCM3 Gene, Allele A: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTCCTTGAAATCGGACGTACC

RCM3 Gene, Allele B: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTCCTTGAAATCGGACGTACC

Research Subject 15 - Novelty-Seeking Score = 35

CTM1 Gene, Allele A: AGGCTCACACACACATTGGC

CTM1 Gene, Allele B: AGGCTCACACACATTGGC

RCM3 Gene, Allele A: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTCCTTGAAATCGGACGTACC

RCM3 Gene, Allele B: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTCCTTGAAATCGGACGTACC

Copymaster 4.4
Group 2B Research Subjects:
Genotypes and Low Novelty-Seeking Scores

Research Subject 16 - Novelty-Seeking Score = 37

CTM1 Gene, Allele A: AGGCTCACACACACATTGGC

CTM1 Gene, Allele B: AGGCTCACACACATTGGC

RCM3 Gene, Allele A: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTAGTCCTTGGAAATCGGACGTACC

RCM3 Gene, Allele B: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTAGTCCTTGGAAATCGGACGTACC

Research Subject 17 - Novelty-Seeking Score = 36

CTM1 Gene, Allele A: AGGCTCACACACACATTGGC

CTM1 Gene, Allele B: AGGCTCACACACATTGGC

RCM3 Gene, Allele A: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTAGTCCTTGGAAATCGGACGTACC

RCM3 Gene, Allele B: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTAGTCCTTGGAAATCGGACGTACC

Research Subject 18 - Novelty-Seeking Score = 35

CTM1 Gene, Allele A: AGGCTCACACACACATTGGC

CTM1 Gene, Allele B: AGGCTCACACACATTGGC

RCM3 Gene, Allele A: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTAGTCCTTGGAAATCGGACGTACC

RCM3 Gene, Allele B: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTAGTCCTTGGAAATCGGACGTACC

Research Subject 19 - Novelty-Seeking Score = 33

CTM1 Gene, Allele A: AGGCTCACACACACATTGGC

CTM1 Gene, Allele B: AGGCTCACACACATTGGC

RCM3 Gene, Allele A: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTAGTCCTTGGAAATCGGACGTACC

RCM3 Gene, Allele B: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTAGTCCTTGGAAATCGGACGTACC

Research Subject 20 - Novelty-Seeking Score = 36

CTM1 Gene, Allele A: AGGCTCACACACACATTGGC

CTM1 Gene, Allele B: AGGCTCACACACATTGGC

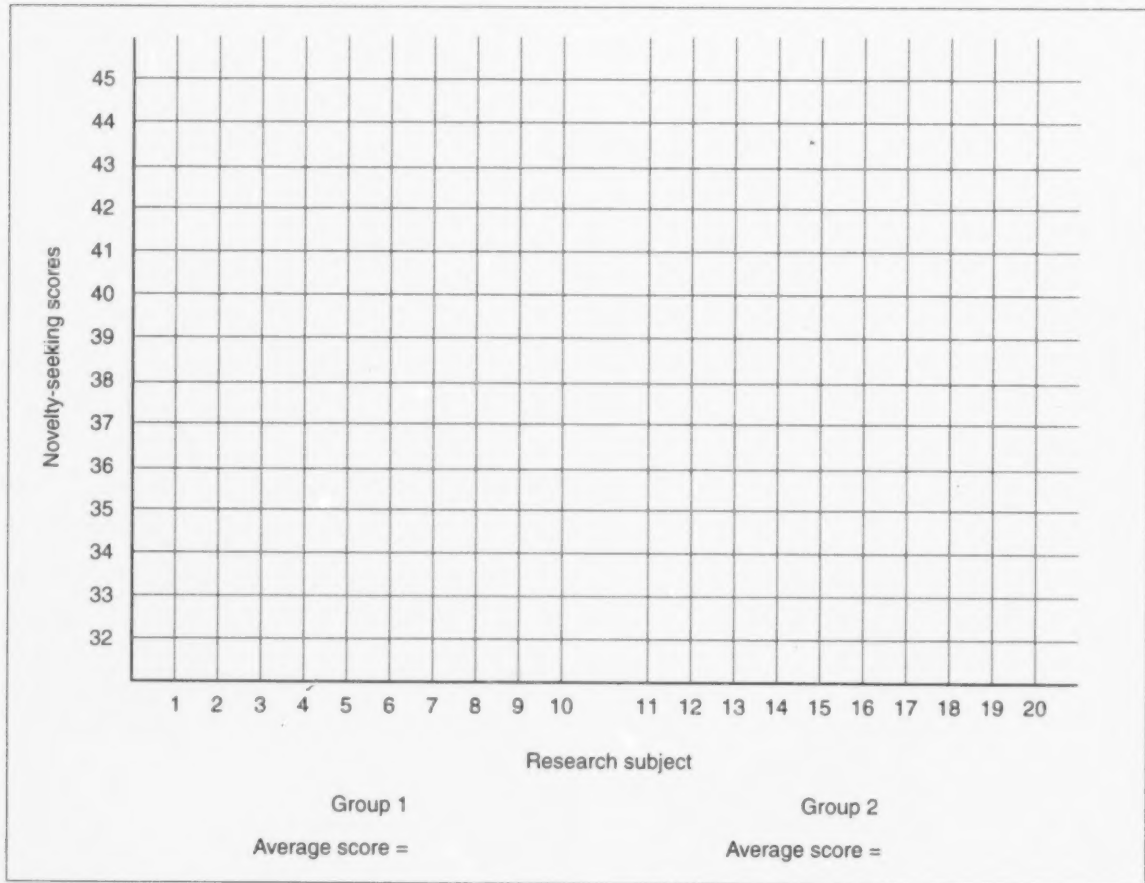
RCM3 Gene, Allele A: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTAGTCCTTGGAAATCGGACGTACC

RCM3 Gene, Allele B: TTACGTTGACCACTGGACCCAGTAGTAGTAGTAGTAGTCCTTGGAAATCGGACGTACC

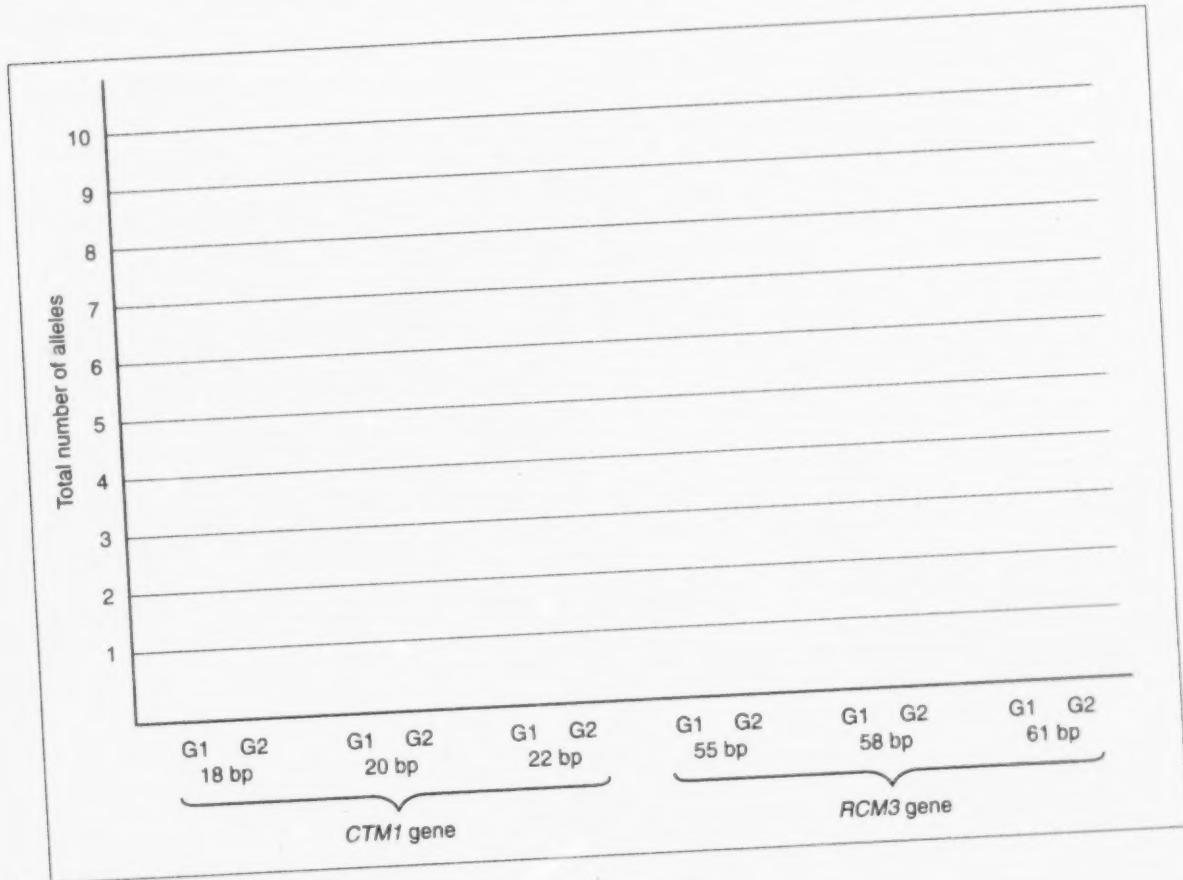
Copymaster 4.5 **Gel Template Sheet**

Group 1												Group 2									
Research subject												Research subject									
1 2 3 4 5 6 7 8 9 10												11 12 13 14 15 16 17 18 19 20									
CTM1 gene	22 bp																				
	20 bp																				
	18 bp																				
Number of 22-bp alleles = Number of 20-bp alleles = Number of 18-bp alleles =												Number of 22-bp alleles = Number of 20-bp alleles = Number of 18-bp alleles =									
Research subject												Research subject									
1 2 3 4 5 6 7 8 9 10												11 12 13 14 15 16 17 18 19 20									
RCM3 gene	61 bp																				
	58 bp																				
	55 bp																				
Number of 61-bp alleles = Number of 58-bp alleles = Number of 55-bp alleles =												Number of 61-bp alleles = Number of 58-bp alleles = Number of 55-bp alleles =									

Copymaster 4.6
Graph Template for Novelty-Seeking Score Data



Copymaster 4.7
Histogram Template for Allelic Frequencies



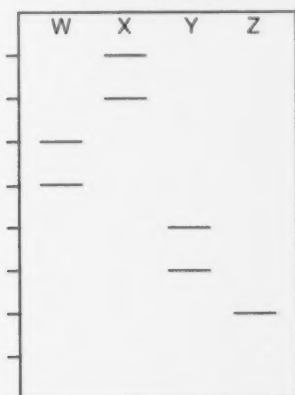
Copymaster 5.1
Reasons in Favor of and Against Paula's Law

In favor of legislation	Against legislation

Copymaster 5.2 Applegate Genotype Results

Gel electrophoresis results from the PCR tests
conducted on all four risk genes

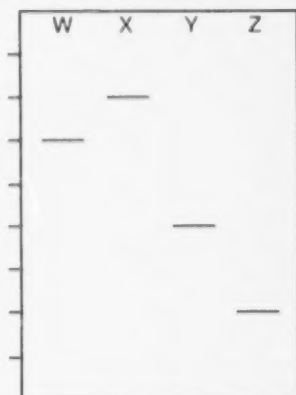
Marcia Applegate



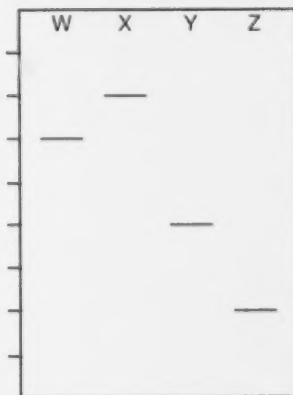
Senator Applegate



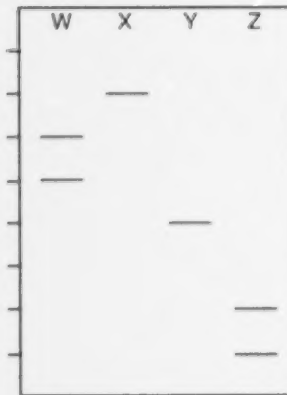
Paula Applegate



Bob Applegate



Henrietta Applegate



Classroom Activities: Student Pages

Activity 1

Investigating Complex Traits

In this first activity you will begin to think about the biology of human behavior. Read the fictitious newspaper article shown in Figure 1.1 that describes the announcement of a gene that determines human

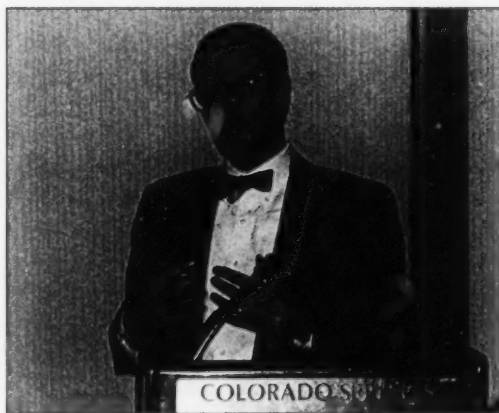
intelligence. Although you may not think of intelligence as a behavior, it is considered one by behavioral geneticists. Use your knowledge of Mendelian genetics to answer the Analysis Questions 1-7.

The Gotham Daily Herald

Special Edition

January 1, 2000

Late Breaking News: Gene for Intelligence Discovered!



Dr. I.Q. Cerebrum announces the discovery of the intelligence gene.

BOSTON. Yesterday, scientists made the startling announcement that they have located a single gene that accounts for human intelligence. Almost unbelievably, this one gene appears to determine the degree of intelligence that any given individual will have in his or her lifetime. The intelligence gene has only two different alleles. Researchers are testing the hypothesis that the intelligence trait shows a codominant inheritance pattern.

Figure 1.1 Late Breaking News article.

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Analysis questions

1. What is intelligence and how is it measured?
2. How do our peers assess our intelligence?
3. If the researchers' hypothesis is correct—that inheritance of intelligence is codominant—how many phenotypes would you observe in the population? What would the phenotypes be?
4. Assume that a student's SAT or ACT score is a valid measure of that student's intelligence. If you reviewed a list of the SAT or ACT scores of all the juniors and seniors in your school, what would you find?
5. Do your school's test scores support the hypothesis that the inheritance of intelligence is codominant? Why?
6. What evidence is there, if any, to suggest that genes contribute to intelligence?
7. What evidence is there, if any, to suggest that the environment contributes to intelligence?

Activity 2

Human Variation



Figure 2.1 Robert Pershing Wadlow (1918–1940) is listed by the Guinness Book of World Records as the tallest person in history at 8' 11".

It is clear that one gene does not determine a person's intelligence. But, if one gene does not determine intelligence, does that mean that genes do not influence intelligence at all? Or, does it mean that the relationship between genes and intelligence might be more complicated? How would you investigate the relationship between genes and intelligence?

Part of the problem with studying intelligence is that it is difficult to define. Intelligence means different things to different people. Let's begin a closer investigation of complex traits with a trait that is easier to define and measure—height.

What is the genetic basis of height? Is height inherited in Mendelian patterns—that is, in the ratios typical of Mendelian traits? How would you determine that? If you were to measure each member of your class, how many phenotypes would you expect to observe? Would you describe the range of phenotypes as narrow or wide? Based on those observations, do you think height is a Mendelian trait?

Clearly, there is a wide range of heights from short to tall and everything in between. If single-gene inheritance does not explain height or intelligence phenotypes, what genetic explanation might?

Geneticists classify height as a trait that shows **continuous variation**. This means that a continuous range of phenotypes is possible. By contrast, a trait like blood type shows **discrete variation**; there are only a few discrete or distinct types: A, B, AB, and O. What other traits show continuous variation? What

might cause certain traits to vary continuously? In many cases, it is the action of two or more genes that causes a trait to show continuous variation. Although you may not have thought much about it, most traits display continuous variation. In fact, other than the blood groups and certain Mendelian disorders, few traits show discrete variation. Even the common example of eye color, where the gene responsible for brown is supposedly dominant to that for blue, is incomplete because it fails to account for the shades of color, such as green, hazel, grey, and others.

The first part of this activity will demonstrate how several genes can act together to contribute to height. The second part of the activity will demonstrate that genes are not the whole story; nongenetic factors also influence height and other continuous traits. You should be aware that this separation of the genetic and environmental influences on height is an artificial one required to perform the activity. In the real world, genes and environment are inextricably linked.

Part I: Modeling Genetic Influence

Assume that there are six genes in the human genome that play a role in influencing how tall a person will become. Each gene is on a separate autosome (nonsex chromosome), and there are two alleles for each gene. You will use two different colors of small beads to represent the two alleles of each gene. Each allele affects height—one increases it by 2 cm, the other decreases it by 2 cm. Your teacher knows the effect of each color and will provide that information to you later.

Because there is evidence that sex chromosomes also have some effect on height, you should compensate for the difference in average height between males and females. For that reason, the activity assumes that a population of females has a starting height of 165 cm and a population of males has a starting height of 175 cm. First, work with a female population to discover how the genes they inherit influence height.

Materials (per student)

- 1 cup containing five red and five white beads
- 2 plastic film canisters, with hole punched through lids; one labeled "Mother" and the other labeled "Father"
- 1 copy of *Human Variation Worksheet—Female*
- 1 copy of *Human Variation Worksheet—Male*

Process and procedures

1. Make sure your cup contains five red and five white beads. Then, reach in without looking,

remove two beads, and place them in your film canister labeled "Mother."

2. Again, without looking, remove two more beads from the cup and place them in your film canister labeled "Father." *These four beads represent your starting parental alleles.*
3. Shake the "Mother" film canister (with your finger covering the hole) and pour out one bead.
4. Shake the "Father" film canister and pour out a second bead. *This pair of beads represents the two alleles of the first of the six genes in the genome of the female that you are modeling.*
5. Record the color combination of the pair of beads in the column next to "Gene 1" in the *Human Variation Worksheet—Female*.
6. When finished, place all four beads back into your cup.
7. Repeat Steps 1–6 five more times.
8. Now repeat the process using a male genome. Repeat Steps 1–6 six times until you have recorded all the data in the appropriate spaces in the *Human Variation Worksheet—Male*.

Part II: Modeling Environmental Influence

Geneticists refer to height as a **polygenic trait** (a trait that is influenced by *many genes*). You modeled polygenic inheritance in Part I, but to see the effects of those genes, you must consider more than just the genes themselves. What else might influence height? In Part II, you will see why geneticists classify height not only as polygenic but also **multifactorial**, which means that a trait is influenced by environmental as well as genetic factors.

To model how environmental factors interact with genes to influence height, you again will use small beads. This time, however, the beads will represent environmental factors, not alleles. Keep in mind that the same environmental factor can influence growth (and other human traits) differently at different stages of life. For example, poor nutrition in childhood can stunt a child's height, but poor nutrition in adulthood has no effect on height. Thus, the timing of environmental factors affects human development.

For this activity, we divide the development of height into three developmental stages: prenatal, childhood, and adolescence. A variety of environmental factors can affect prenatal (fetal) growth, such as maternal cigarette smoking and alcohol abuse. Those factors increase the risk of intrauterine (within the uterus) growth retardation and a variety of other problems, including respiratory distress and feeding difficulties. Can you think of other factors that might influence growth during childhood and adolescence?

As in Part I, your teacher has information as to what influence each different colored bead has on height, and will share it with you later.

Materials (per student)

- 1 plastic film canister, with hole punched in lid
- 1 each of orange, yellow, green, and blue beads
- 1 copy of *Human Variation Worksheet—Female* from Part I
- 1 copy of *Human Variation Worksheet—Male* from Part I

Process and procedures

1. Place one orange, yellow, green, and blue bead into a film canister. *The four colors represent different degrees of environmental influence.*

2. Shake the film canister and pour out a single bead. Record its color in the space next to "Prenatal" in the *Human Variation Worksheet—Female*.
3. Replace the bead and repeat Step 2, but record the bead color in the space next to "Childhood."
4. Replace the bead and repeat Step 2 again, but record the bead color in the space next to "Adolescence."
5. Now repeat the process for the male. Repeat Steps 2–4 and record the bead colors in the appropriate spaces in the *Human Variation Worksheet—Male*.
6. Use the values for genetic and environmental influences provided by your teacher to calculate the height of your female and male. Record your results on the worksheet.
7. Follow your teacher's directions and record the heights for your female and male on a class histogram.

Analysis questions

1. What are you simulating by withdrawing four beads from the cup in Part I?
2. Why must you withdraw a pair of beads six times?
3. Describe the distribution, or range, of heights on the class graph. Does the distribution reasonably model actual distributions of height? Explain.
4. Does a single-gene or a multifactorial model better explain the inheritance of height? Why?
5. What type of variation is evident in the class data? What explains this variation and how does it differ from the variation seen in blood types?
6. If you were to combine the data from your class with the data from several other classes, how would the graph of height change? Would the graph provide a better or worse illustration of a continuous variation? Why?

7. Based on the discussion in *Additional Information about Height, Genes, and Environment*, answer the following:

a. What biological factors influence growth? How

are those factors related to or influenced by genes?

b. What environmental factors interact with genetic factors to influence height?

Additional Information about Height, Genes, and Environment

Most human traits, such as weight, shoe size, intelligence, and ability to throw a ball, exhibit a great deal of phenotypic variation. If we measure the arm lengths of many different people, a few will be very long, a few others very short, and most will fall somewhere in between. When this type of continuous distribution is represented graphically, we get the familiar bell-shaped curve seen in Figure 2.2.

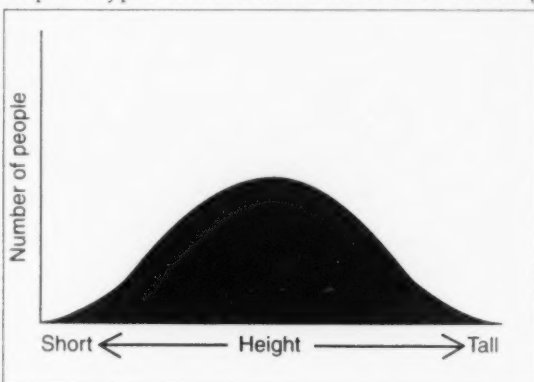


Figure 2.2 Continuous distribution of human heights.

Height is like many other physical traits in which genes and environment are important. Unlike your experience in this activity, however, their effects are not separate in time: first genes, then environment. For the purpose of this modeling exercise, we chose to demonstrate genetic and environmental influences on a "starting height." In reality, there is no starting height. Instead, genes and environment act together to determine how tall you will be. (To a geneticist, environment refers to anything that is not

genetic.) For example, some of your genes encode the instructions that affect how long your legs *could be*, under ideal circumstances. If you break a leg at a growth plate (regions of rapid bone growth during childhood) that leg may never achieve its maximum length. Thus, an injury (an environmental factor) can interfere with the developmental processes initiated by genes.

Another clear example of the interaction of genes and environment in development is nutrition. If your genes encode the potential for a tall, muscular body but you are malnourished as a child, your body will not have the building blocks to achieve its full genetic potential (tall and muscular). For example, the average height of the population of Japan increased by several inches during the early and middle 20th century. This relatively rapid increase in average height was not caused by changes in the genes of the whole population. Rather, it was due to improvements in the diet of successive generations of Japanese children during their growth years.

From the preceding examples, you can see that genes and environment interact during development to produce height in all people. Those same interactions also explain the *differences* in height among particular individuals. Although that distinction might appear trivial, it is not. All biologists recognize that genes and environment interact during development, and developmental biologists try to understand *how* those interactions lead to particular phenotypes (both physical and behavioral). **Behavioral geneticists**, on the other hand, are interested in understanding how genes and environment lead to *differences* in the behavioral phenotypes of individuals (not in how the phenotypes form). To investigate behavioral differences, they study human populations, attempting to sort out the proportion of difference that is due to genes and the proportion of difference due to the environment.

Activity 3

A Novel Trait

It is obvious that certain complex traits, such as intelligence and height, vary within families. In a family with two sons, for example, one may be taller than the father and the mother, whereas the other is taller than the mother but shorter than the father. Despite this variation within families, it also is apparent that the height of children is related to the height of their parents. Tall parents tend to have tall children and short parents tend to have short children. This activity will expand on the idea that genes and environment interact to produce complex human traits that vary among individuals. In this case, however, the complex trait is behavioral, not physical.

You will investigate the contribution that genes and environment make in influencing individual differences in novelty-seeking behavior. Novelty-seeking behavior is the tendency to be interested in and excited by new, and sometimes risky, experiences. Psychologists use traits, such as novelty seeking, anxiety, aggressiveness, and creativity, to define and describe personality. If they can describe personality traits and related behaviors, they can begin to study whether and how much genes might affect those traits. That is what you will begin to do in this activity.

Part I: Novelty-Seeking Survey

Materials (per student)

- 1 blank slip of paper
- 2 sheets of graph paper
- 1 copy of *Novelty-Seeking Survey*
- 1 copy of *Novelty-Seeking Score Data for Fraternal Twins*

Process and procedures

A group of 15-year-old students was involved recently in a personality study that was carried out in the Minneapolis-St. Paul area. The students were asked about behaviors they might have engaged in, and from their answers, each student received a score. The score represents one measure of an individual's tendency to engage in novel (new), or risky, experiences.

To begin this activity, you will complete a similar survey modeled after those used in behavioral research. To ensure confidentiality, do not write on the survey itself, but rather keep a tally of your "yes" answers on a separate piece of paper. Do not write your name on the survey or on the slip of paper with the number of your "yes" answers.

1. Complete the survey distributed by your teacher. **Complete both pages of the survey.** Your answers will remain anonymous.
2. Total the number of "yes" answers from your responses and record that number on the slip of paper.

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Student Pages

3. Fold the slip of paper and give it to your teacher.
4. When your teacher asks, predict what the range of your classmates' scores might be. Assist your teacher in developing a graph of the range of class scores.

Analysis questions

1. Describe the distribution of scores (the shape of the graph). *Hint: What is the approximate average score? Did everyone have the same score? What type of variation is evident?*
2. How might you explain that distribution of scores?
3. Do you think the survey is an accurate way to measure the risk-taking (or novelty-seeking) aspects of an individual's personality? Why? If you answered no, suggest a better measure.
4. Think back to the height analysis that you performed earlier. How did you explain variation in height?
5. Is it reasonable to propose that we can explain variation in personality traits the same way we explain variation in height? Explain.
6. Do you think your total score would be different if you took the survey at ten years old or forty-five years old?

Part II: Data from Minneapolis-St. Paul Study

The group of students from Minneapolis-St. Paul was chosen to participate in the novelty-seeking study because each student was a member of an identical twin pair. Furthermore, each pair of twins was separated shortly after birth, adopted, and raised in different families (so-called *adopted-away twins*).

Process and procedures

1. What biological characteristics of identical twins make them interesting subjects for studies of complex traits?
2. If identical twins are adopted and raised apart, would you expect them to experience the same environmental influences? Why is that important in studies of genetics?
3. Make a list of attributes that identical twins might be more likely to share than if they were same-sex, fraternal (nonidentical) twins. (Fraternal twins are only as similar genetically as nontwin brothers or sisters; they just happen to be the same age.)

Suppose you are a scientist studying the novelty-seeking trait measured earlier. You would like to measure the adopted-away identical twin of each of the twenty students currently involved in your research.

4. Would you expect the identical twins of those twenty students to have scores similar to or different from their co-twins?

5. How would you test your hypothesis?
6. When the novelty-seeking test was administered to the adopted-away co-twin of each student tested earlier, scientists obtained the results in Table 3.1. Read the section *Using and Interpreting Scatterplots* before proceeding to the next step.

Table 3.1 Novelty-Seeking Scores of Adopted-Away Identical Twins

Identical Twin Pair	Score of Twin 1	Score of Twin 2
A	37	37
B	39	38
C	40	40
D	37	35
E	40	43
F	40	36
G	39	39
H	38	36
I	40	37
J	37	41
K	40	37
L	40	41
M	34	37
N	36	36
O	41	41
P	37	40
Q	42	42
R	37	34
S	43	40
T	31	34

Using and Interpreting Scatterplots

The scatterplot diagram is a tool for illustrating the relationship between pairs of variables (such as the relationship between data from twin pairs). To graph data for a twin pair, first find the novelty-seeking score for Twin 1 on the x-axis of Figure 3.1 and extend a vertical line up from that point. Next, find the score for Twin 2 on the y-axis and extend a horizontal line from that point. At the intersection of the two lines, place a dot on the graph. Continue that process until there is a point for each pair of twins.

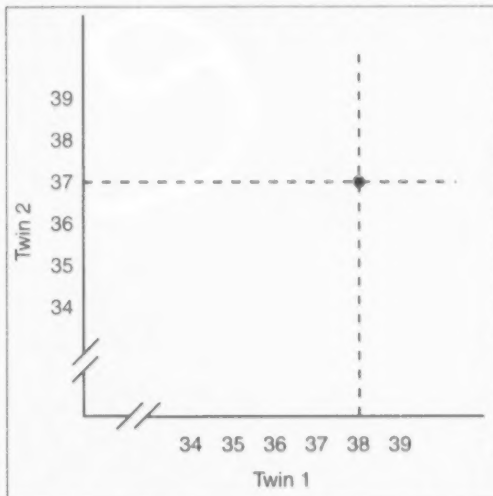


Figure 3.1 Each data point on the scatterplot represents the intersection of values for a twin pair.

The pattern formed by the points on the scatterplot provides a visual representation of the strength of the association between the pairs of values (for Twin 1 and Twin 2, in our examples). If the association is very strong (and in a positive direction), the points will tend to cluster around a diagonal line extending from the bottom left to the top right of the graph. That is because when one twin has a high score, the co-twin is likely to have a high score as well; when one twin has a low score, the co-twin is likely to have a low score; and so on. As the association becomes weaker, the points will show more and more deviation from a straight line. Another way of interpreting this "scatter" or deviation is that the ability to predict one score in a pair from the other score is less than perfect. When there is no association, there will be no linear trend apparent at all, and the points will appear as a somewhat circular pattern. If the association is inverse (that is, when the value of one observation is high, the second observation will be low), another linear relationship will be seen, this time extending from the top left to the bottom right of the graph.

7. Graph those results by placing a dot where the value of the score for Twin 1, found along the x-axis, intersects the value of the score for Twin 2, found along the y-axis. There will be only one dot for each pair of twins.
 - a. Around what values do the greatest number of scores cluster?
 - b. How would you describe the relationship between a particular twin's score and his or her identical co-twin?
8. Predict the results if this same kind of comparison were made between the twins' heights.
9. Examine the height graph for identical twins displayed by your teacher.
 - a. Around what values do the greatest number of heights cluster?
 - b. How would you describe the relationship between a particular twin's height and that of his or her co-twin?
 - c. Is the association between twin pairs stronger for novelty-seeking behavior or for height? Explain.
10. Geneticists conducted a similar test of novelty seeking and height on a group of fraternal twins (not identical) who also were adopted and raised apart. Would you expect those fraternal twins to be more or less similar to each other for height than the identical twins were to each other? Why? What about novelty seeking?
11. Use the novelty-seeking scores distributed by your teacher to graph the results from the novelty-seeking study of the fraternal twins.

Analysis questions

1. Compare the heights for the fraternal twins in Figure 3.2. What similarities and differences do you notice when you compare those data with the data from the identical twins?

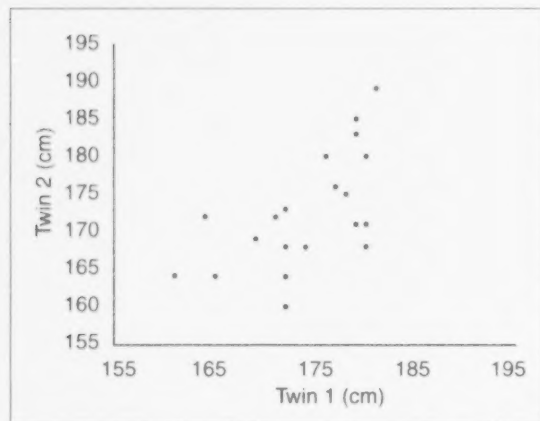


Figure 3.2 Scatterplot of heights for fraternal twins.

2. How would you explain the similarities and differences?
3. Compare the novelty-seeking graphs for the identical and fraternal twins. What similarities and differences do you notice?

4. Would you explain the similarities and differences the same way you did for height?
5. Based on these data, is it reasonable to conclude that genes influence height? Explain your response. Based on these data, is it reasonable to conclude that genes influence novelty-seeking behavior? Explain your response.
6. Based on these data, is it reasonable to conclude that the environment influences height? Explain your response. Based on these data, is it reasonable to conclude that the environment influences novelty-seeking behavior? Explain your response.
7. Based on the phenotypic variation that you observed for the personality trait of novelty seeking, would you expect one or many genes to be involved? Explain.
8. If you agree that novelty-seeking behavior is affected by genes and the environment, you agree that novelty seeking is a multifactorial trait. What environmental factors might affect novelty seeking?
9. Is it likely that novelty seeking is unique, or would you also expect other human behaviors to be influenced by genes? If yes, which behaviors?

Additional Information about Novelty Seeking, Survey Methods, and Scatterplots

In this activity, you completed a "self-report questionnaire" about novelty seeking. Psychologists use self-reporting questionnaires often to describe personality. Perhaps surprisingly, those questionnaires are quite reliable. One way to increase reliability is to ask the same question in several ways. That minimizes the likelihood that survey results will be skewed because a subject misunderstands one question. Although the survey you completed in this activity is not an actual personality survey (because of legal concerns), it does give you some idea of the redundancy intentionally built into surveys of this type. The survey you used has not been designed for actual research on novelty seeking. You should draw no conclusions about your personality from your score.

Several of the questions deal with issues of risk that also are related to issues of integrity and honesty. Driving a car 100 mph is illegal and risky; there usually are negative consequences to excessive speeding. Bungee jumping, especially if it is completely legal, may appear to be pure risk, with no related integrity issues. Even pure risks, however, may have integrity implications that depend on the circumstances of the risk taker. For example, some would agree that a father of five is irresponsible if he bungee jumps, whereas a 15-year-old is simply indulging his or her natural appetite for thrills.

In any case, the activity of bungee jumping arises from a desire or tendency to do something that produces a thrill. The feelings of desire and satisfaction that result are emotions or thoughts in the brain, and the brain stores these emotions in its cellular and biochemical structure. Thus, the behavior itself has a physical component. Of course, our free will and decision-making ability allow us to moderate our behavioral traits more than our physical traits, such as height and blood type.

The scatterplots used in this activity are graphic representations of correlations. A **correlation** is a statistic that indicates the degree of association between two variables. A value of +1 is a complete positive association, a value of 0 indicates no association, and a value of -1 indicates a complete inverse (or negative) association. The correlations in the scatterplots from Activity 3 have been calculated as follows: 0.97 for height in identical twins; 0.61 for height in fraternal twins; 0.60 for novelty-seeking score in identical twins; and 0.23 for novelty-seeking score in fraternal twins.

When you see newspaper articles report that IQ is about 50 percent genetic, that does not refer strictly to correlation. Instead, it means that 50 percent of the difference in IQ in a population is due to genetic factors. It does not mean that 50 percent of *your* IQ or your teacher's IQ is genetic. Your IQ (which is the measure of your ability to perform well on specific tests) may be more than 50 percent due to your genes or less than 50 percent. The number reported is a population average called **heritability** (H), which is calculated as the proportion of phenotypic variation (V_P) that is due to genotypic (or genetic) variation (V_G).

heritability = genotypic variation $\div$ phenotypic variation, or mathematically:

$$H = V_G \div V_P$$

Phenotypic variation is a combination of genetic and environmental variation (V_E).

Phenotypic variation = genotypic variation + environmental variation, or

$$V_P = V_G + V_E$$

Keep in mind that genes and environment interact ($V_G \rightleftharpoons V_E$). Height is a complex trait that has one of the highest heritabilities ever measured. For height, $H = 80\text{--}90$ percent, which means that 80–90 percent of the height differences in a population are due to genetic variation.

Activity 4

Finding the Genes That Influence Novelty-Seeking Behavior in Humans

From your study of the trait of novelty seeking among identical and fraternal twins, do you think it is reasonable to expect that genes are involved in that behavior? What evidence is there that the environment also plays a role? If you wanted to try to identify the genes involved in novelty seeking, how would you go about it?

In this activity, you will model a technique that behavioral geneticists use when searching for genes that influence complex traits such as novelty seeking. Actual experiments of this type require blood or tissue samples so that DNA can be extracted. You will not collect blood samples or real DNA. You will model, however, the same type of procedures and analysis that scientists would perform.

Materials (per student)

- 1 copy of *Research Subjects: Genotypes and Novelty-Seeking Scores* from your teacher
- 1 copy of *Gel Template Sheet*
- 1 copy of *Graph Template for Novelty-Seeking Score Data*
- 1 copy (per team) of *Histogram Template for Allelic Frequencies*

Process and procedures

Imagine that you are planning your search for potential genes involved in novelty-seeking behavior. Because the distribution of novelty-seeking scores shows continuous variation, you suspect that several genes might be involved, as well as various environmental factors. Thus, it is possible, perhaps even likely, that any individual gene might exert

only a small effect on behavior. How would you search for genes that exert minor influence?

One way is to compare directly the DNA of people who possess the trait with those who do not. Of course, that raises the question, Who "has" the trait when the trait is continuously distributed? One approach is to use two groups of people: one with very high scores for the trait and one with very low scores for the trait, so that there is little or no overlap between the two groups. If people who possess a behavioral trait at one extreme end of a phenotypic range have DNA sequences that are different from those found in people at the other end, then those sequence differences might correspond to alleles or genes that influence the behavior. This type of experiment is called an association study because

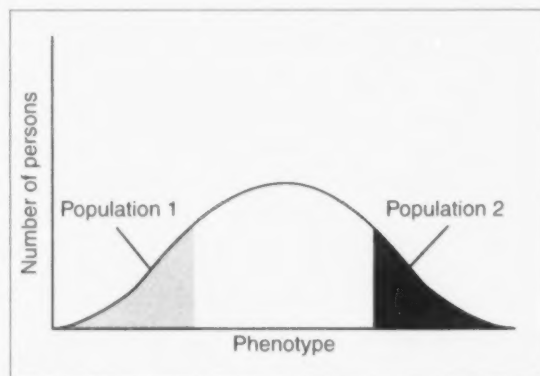


Figure 4.1 The rationale behind an association study: Do these two populations have any consistent differences in their DNA?

researchers are searching for an association between a behavior and a particular DNA sequence.

Association studies are limited in humans and animal models by how well we can define and measure the phenotype being studied. For example, if the novelty-seeking surveys are not good measures of novelty-seeking behavior (however we define that phenotype), then the scores derived from those surveys are invalid. Any associations between different alleles and those scores would become meaningless, at least for novelty-seeking behavior.

Association studies also cannot account for all of the genetic factors and environmental influences that affect a behavior. In this sense, they can give an incomplete or oversimplified picture of the causes of behavior. For example, any subject that does not fit the pattern provides evidence that the allele under consideration is not required for that behavior. The power of association studies is limited by the number of subjects involved in the studies. Finding genes of small effect may require many hundreds or even thousands of subjects.

Finally, association studies only test genes or markers that are chosen for study by the researcher, often based on prior information. For example, a gene might be chosen because it is known to code for a neurotransmitter that plays a role in brain response. Other methods such as linkage analysis are often used for more exploratory studies designed to detect new, previously unidentified genes.

1. Choose at random a sheet of paper from a container provided by your teacher. Each sheet lists five research subjects, along with the sequences of two different alleles for two genes (*CTM1* and *RCM3*). These genes may or may not be associated with novelty-seeking behavior. Each sheet also lists the novelty-seeking score for each research subject.
2. Working individually, count the number of bases present in each of the alleles for each of your research subjects. Then plot each allele on the *Gel Template Sheet*. Under the number of each research subject, draw a line at a position indicating the length of each allele (see example in Figure 4.2). In some cases, both alleles may be the same size and so you will draw only a single line. Remember that this represents two alleles in a homozygous

condition: one that was inherited from the father and one from the mother. When you are finished, you will have the genotype pattern for your research subjects.

3. Now plot the novelty-seeking scores for your five research subjects on the *Graph Template for Novelty-Seeking Score Data*.
4. Form teams of two according to your teacher's instructions. Share with your teammate the genotypes and novelty-seeking scores for each of your subjects. Record that information on your *Gel Template Sheet* and *Graph Template for Novelty-Seeking Score Data*. When finished, you should have the genotypes and novelty-seeking scores for the ten research subjects in your group.
5. Next, form teams of four according to your teacher's instructions. Share data with all team members as in Step 4. When finished, each team member should have a complete data set of genotypes (on the *Gel Template Sheet*) and novelty-seeking scores (on the *Graph Template for Novelty-Seeking Score Data*).
6. Create a histogram that shows the frequency of each allele type in each group. Use the *Histogram Template for Allelic Frequencies*. Then, calculate the average novelty-seeking score for both your groups (Group 1: subjects 1–10; Group 2: subjects

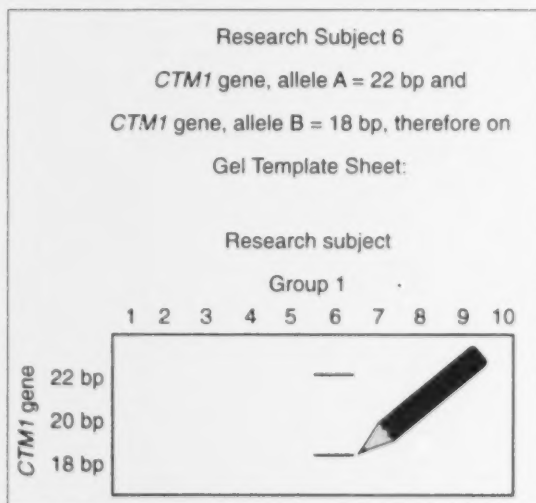


Figure 4.2 Plotting the number of base pairs for an allele on the *Gel Template Sheet*.

What Are Short Tandem Repeats?

What seems to determine the differences in the lengths of the two alleles for the *CTM1* and *RCM3* genes? These length differences are due to the number of copies of short repeated sequences found in the middle of each region of interest. These variations are called short tandem repeat polymorphisms (STRs) and are the same types of repeats found in some genes associated with disease, such as Huntington disease or fragile X syndrome. Those disorders are caused by a great increase in the normal number of trinucleotide repeats found within those genes. The presence of the extra repeats leads to a nonfunctional gene product. For *CTM1*, the repeat is CA (a dinucleotide) and for *RCM3* the repeat is AGT (a trinucleotide).

In a real laboratory, the differences in length would be determined by first multiplying the DNA sequence of interest using a technique called the polymerase chain reaction (PCR). In PCR, two short DNA molecules called primers are used to bracket the DNA sequence to be copied. The PCR reactions produce a large number of DNA molecules that are exact matches for the DNA sequence located between the two primer sequences. For example, in this activity, the primer sequences for the *CTM1* gene are AGGCT at one end and GCCAA at the other end. After the PCR reactions are completed, the multiplied DNA fragments are separated by size using another technique called gel electrophoresis. After staining the gel with a chemical dye, the DNA fragments can be visualized and photographed. *Hint: The section Additional Information about PCR Analysis, which is located at the end of this activity, will help you understand how the process works. You are simulating the results of this analysis by drawing lines corresponding to the lengths of DNA fragments in the appropriate positions on the gel template.*

11–20). Record the scores in the space provided on the *Graph Template for Novelty-Seeking Score Data*. *Hint: Remember some research subjects who display only one band actually have two alleles of the same size.*

Analysis questions

1. Can DNA polymorphisms that lie outside the coding regions of genes be useful to scientists hunting for genes that influence behavior?
2. What criterion did scientists use when assigning research subjects to Group 1 and Group 2? Why do you think the subjects were organized in this way? Would a random population make it easier or more difficult to identify potential genes involved in novelty seeking?
3. What is the relationship between the *RCM3* allele 61 and the novelty-seeking scores? Explain whether that relationship offers evidence that a particular gene might influence novelty-seeking behavior.
4. What is the relationship between the *RCM3* alleles 55 and 58 and the novelty-seeking scores? Explain whether those relationships offer evi-

dence that genes might influence novelty-seeking behavior.

5. Do the data provide reasons for caution as to the role that *RCM3* allele 61 plays in influencing novelty-seeking behavior? Use specific examples from the data to defend your answer. What other factors might be important in novelty-seeking behavior?
6. What is the relationship, if any, between the *CTM1* gene and novelty-seeking behavior?
7. *Challenge:* What additional studies might behavioral geneticists perform to test their hypothesis that *RCM3* allele 61 influences high novelty-seeking behavior?

Extension: Behavioral geneticists use statistical analysis to test whether relationships between two variables are likely to be significant or merely due to chance. Why might that be important? Your teacher may elect to have you perform an extension activity in which you learn to perform a chi-square analysis to test whether differences observed in allele frequencies are significant in a formal statistical sense.

Additional Information about PCR Analysis

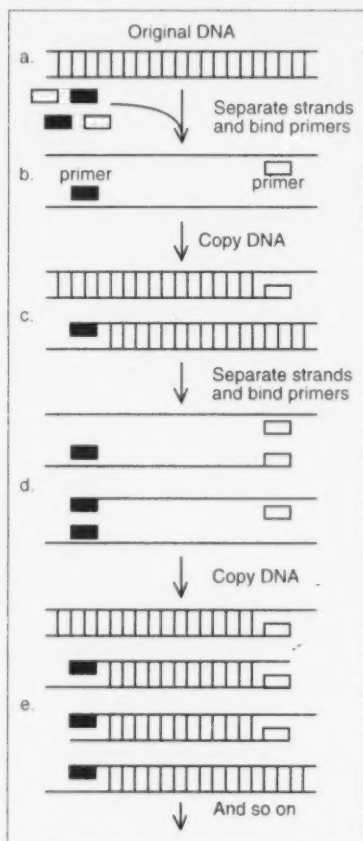


Figure 4.3 The polymerase chain reaction (PCR) starts with double-stranded template DNA and nucleotide primers that are complementary to sequences at the ends of the fragment to be duplicated. Because of the orientation of the primers, DNA products of previous rounds act as templates in subsequent rounds. At each round, the amount of target DNA is doubled.

Large DNA fragments have trouble moving through the pores in the gel and migrate slowly. Smaller fragments have an easier time and migrate more quickly.

The sizes of the amplified DNA fragments can be estimated by comparing them to size standards, which are simply DNA fragments of known size. (Note that the spacing between different-sized fragments is not regular. That has to do with the physics of how DNA molecules move through the gel.)

Molecular biologists analyze DNA molecules by size, sequence, or both. When little is known about genes that might influence a behavioral trait, size comparisons of DNA fragments can be used to search for possible associations. Since the late 1980s, an easy way to perform such an analysis has been to use the polymerase chain reaction (PCR) to amplify (produce a large amount of) DNA from a region of the chromosome or gene that you want to study. Figure 4.3 illustrates this technique. Following the PCR reactions, gel electrophoresis is used to sort the DNA fragments by size. Scientists compare fragment sizes across samples, looking for specific sizes called polymorphisms that are found in association with the trait being studied. You simulated that process by counting the number of DNA bases in your fragments and drawing them on the gel templates.

Gels for electrophoresis are made from agarose (a carbohydrate from seaweed) or polyacrylamide (a synthetic polymer). In either case, the gel contains pores or spaces, like a sieve, through which the DNA fragments can move. Each DNA sample is loaded with a micro-pipet into a separate sample well located at one end of the gel.

To separate the DNA fragments, scientists apply an electrical current to the gel. A force must be applied to the gel to move the DNA out of the sample wells and into the gel itself. An electrical current is effective because DNA is an acid, which is negatively charged at neutral pH. Therefore, DNA samples are loaded at the end of the gel toward the negative electrode.

Under the force of the electrical current, the DNA fragments migrate into and through the gel matrix toward the positive electrode.

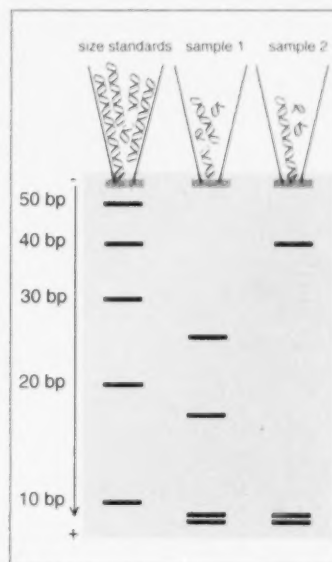


Figure 4.4 In gel electrophoresis, mixtures of DNA fragments are placed into separate wells of a gel (a thin slab of a gelatinlike substance). When an electric current is run through the gel, the negatively charged DNA fragments migrate through the gel toward the positive electrode. The length of each fragment determines how quickly it moves, so the procedure separates the fragments by size.

Activity 4 Extension: Chi-Square Calculation

Sometimes it is not obvious whether allele frequency differences between groups reflect real differences in populations or result from fluctuations due to chance. For example, there are slight differences in the allele frequencies for *CTM1* in Activity 4. Is a frequency of six alleles out of twenty in Group 1 (high novelty seeking) and eight alleles out of twenty in Group 2 (low novelty seeking) for the 22-bp allele a real difference or just a chance difference? The frequencies of the 61-bp allele of *RCM3* (ten alleles of twenty in the high-scoring group and two alleles of twenty in the low-scoring group) are more dramatically different. In both cases a formal statistical test can establish whether the differences are likely to be real or likely to occur by chance.

The chi-square statistic provides a way to evaluate differences between groups in a formal manner. This test (developed by the prominent statistical geneticist Karl Pearson approximately a century ago) compares the frequencies that are observed in a set of data to the frequencies that would be expected just by chance. This test is often referred to as a "goodness-of-fit" test because it tests how well our observations fit the predicted outcome.

As a simple example, consider the results of a coin toss when a balanced coin is tossed 100 times. By chance alone we would expect it to come up heads about 50 times and tails about 50 times. How far from the 50-50 prediction of heads and tails could our actual observations be and still fit our predicted outcome? Are 45 heads and 55 tails significantly different from the 50-50 split? What about 40 heads and 60 tails? 70 heads and 30 tails? At what point would we conclude that there was some variable in our coin-toss experiment that was causing heads (or tails) to deviate in a real way from the expected frequency distribution? The chi-square test provides a way to make that decision. First, we must decide what level of significance is suitable for our needs. Typically, scientists use a 5 percent level of significance, which means that only 1 time in 20 would we expect to see such a large deviation due to chance alone. (In fact, a distribution of 39 or fewer heads and 61 or more tails, or vice versa, would be a significant deviation from chance at the 5 percent level of significance.)

In Activity 4, we have a slightly more complex situation than a simple coin-toss experiment. There are two groups (high and low scorers), defined on the basis of their novelty-seeking scores and three alleles in each group for each gene. If we evaluate the genes *CTM1* and *RCM3* separately, we can summarize the observed allele frequencies in a 2×3 table called a *contingency table*. Applying this method to the *RCM3* gene, we find the following frequencies.

Table 4.1 Observed Allele Frequencies for the *RCM3* Gene

Frequency	61 bp	58 bp	55 bp	Row Total
High	10	4	6	20
Low	2	8	10	20
Column Total	12	12	16	40

The expected frequencies can be calculated from the numbers in the row and column totals. This comes from the law in probability theory that the chance that two or more independent events will occur together is the product of their chances of occurring separately. To apply this law in a chi-square analysis, use the following formula:

$$\text{Expected frequency} = \frac{\text{row total} \times \text{column total}}{\text{total sample size}}$$

Calculate the expected frequencies for the contingency table:

allele 61/high	=	(20)(12) ÷ 40 =	6
allele 58/high	=		—
allele 55/high	=		—
allele 61/low	=		—
allele 58/low	=		—
allele 55/low	=		—

Place your calculated expected frequencies in the following table:

Table 4.2 Expected Allele Frequencies for the *RCM3* Gene

Frequency	61 bp	58 bp	55 bp	Row Total
High	6	—	—	20
Low	—	—	—	20
Column Total	—	—	—	40

The chi-square value (χ^2) for the set of data is then calculated using the following formula:

$$\chi^2 = \sum (\text{observed number} - \text{expected number})^2 \div \text{expected number}$$

The formula states that chi square is calculated by squaring each difference between the expected frequency and the actual observed frequency for each cell in the contingency table. Each difference squared is then divided by the expected number for that cell. The quotients are then added together to get the chi-square value.

Use the formula to calculate χ^2 for the *RCM3* gene. Note there are six terms to add, one for each square in our contingency table.

$$\chi^2 \text{ for } 61/\text{high} = (10 - 6)^2 \div 6 = 4^2 \div 6 = 16 \div 6 = 2.67$$

$$\chi^2 \text{ for } 58/\text{high} = \underline{\hspace{2cm}}$$

$$\chi^2 \text{ for } 55/\text{high} = \underline{\hspace{2cm}}$$

$$\chi^2 \text{ for } 61/\text{low} = \underline{\hspace{2cm}}$$

$$\chi^2 \text{ for } 58/\text{low} = \underline{\hspace{2cm}}$$

$$\chi^2 \text{ for } 55/\text{low} = \underline{\hspace{2cm}}$$

Total χ^2 value $\underline{\hspace{2cm}}$

The calculated chi-square value is next compared to others in a table of critical values to determine if it is significant. To look up a chi-square value, you first must determine the *degrees of freedom*. In a two-way contingency table, the degrees of freedom are equal to $(r - 1)(c - 1)$, where r is the number of rows in the contingency table and c is the number of columns in the contingency table. For our *RCM3* example, the degrees of freedom are $(2 - 1)(3 - 1) = 2$.

Once the value of chi square and the degrees of freedom are known, they are compared to the critical values that can be found in a table of chi-square critical values, available in most statistical textbooks. These are usually listed as critical values for a set of probability or p -values. A p -value relates to the level of significance discussed earlier. It refers to the probability that the difference between the observed and expected frequencies is due to chance. For example, a p -value of 0.05 means that a difference at least as big as that observed in the experiment would occur by chance 1 in 20 tries. Using a p -value of 0.01 means a dif-

ference that large or larger would occur by chance only 1 in 100 tries. Traditionally, a p -value of 0.05 or smaller is used to indicate a significant finding; larger values are considered to indicate nonsignificant findings.

The chi-square value calculated for *RCM3* is 7.68 and our example has 2 degrees of freedom. Using the table below, you can see that the critical values of chi square for 2 degrees of freedom are 5.99 at $p = 0.05$ and 9.21 at $p = 0.01$. Because 7.68 lies between 5.99 and 9.21, the deviation from chance association between allele type and group (high and low scorers) for *RCM3* is statistically significant at $p < 0.05$. In other words, the link between novelty-seeking scores and the allele types for *RCM3* is stronger than we would expect from just chance alone.

Table 4.3 Excerpt from a Chi-Square Table

Degrees of Freedom	p -values			
	0.10	0.05	0.01	0.005
1	2.71	3.84	6.63	7.88
2	4.61	5.99	9.21	10.60
3	6.25	7.81	11.34	12.84
4	7.78	9.49	13.28	14.86

Similar calculations can be made for gene *CTM1*. The observed frequencies are as follows.

Table 4.4 Observed Allele Frequencies for the *CTM1* Gene

Frequency	22 bp	20 bp	18 bp	Row Total
High	6	7	7	20
Low	8	6	6	20
Column Total	14	13	13	40

The expected frequencies can be calculated as before. For each cell in the contingency table, multiply the observed row total by the observed column total and divide by the total sample size.

$$\text{allele } 22/\text{high} = (20)(14) \div 40 = \underline{\hspace{2cm}} 7$$

$$\text{allele } 20/\text{high} = \underline{\hspace{2cm}}$$

$$\text{allele } 18/\text{high} = \underline{\hspace{2cm}}$$

$$\text{allele } 22/\text{low} = \underline{\hspace{2cm}}$$

$$\text{allele } 20/\text{low} = \underline{\hspace{2cm}}$$

$$\text{allele } 18/\text{low} = \underline{\hspace{2cm}}$$

Place your calculated expected frequencies in the following table:

Table 4.5 Expected Allele Frequencies for the *CTM1* Gene

Frequency	22 bp	20 bp	18 bp	Row Total
High	7	—	—	20
Low	—	—	—	20
Column Total	—	—	—	40

The chi-square value is calculated from these observed and expected cell frequencies in the same manner as illustrated here for RCM3. Perform the χ^2 calculation:

$$\chi^2 = \sum (\text{observed number} - \text{expected number})^2 \div \text{expected number}$$

$$\chi^2 \text{ for } 22/\text{high} = (6 - 7)^2 \div 7 = (-1)^2 \div 7 = 1 \div 7 = 0.14$$

$$\chi^2 \text{ for } 20/\text{high} = \text{—}$$

$$\chi^2 \text{ for } 18/\text{high} = \text{—}$$

$$\chi^2 \text{ for } 22/\text{low} = \text{—}$$

$$\chi^2 \text{ for } 20/\text{low} = \text{—}$$

$$\chi^2 \text{ for } 18/\text{low} = \text{—}$$

$$\text{Total } \chi^2 \text{ value} = \text{—}$$

Again using the chi-square table, what does your calculated value for chi square tell you about the association between novelty-seeking scores and any of the allele types for *CTM1*?

Activity 5

Paula's Law

Behavioral geneticists usually speak in terms of risks and probabilities for human populations. Understanding behavioral variation at the level of populations is not the same as understanding variation in individuals. In fact, the use of population data to make inferences or predictions for individuals is inappropriate and often creates problems.

Let's suppose that you are in a population or group at greater risk for causing automobile accidents than other population groups. (That is certainly true if you are a teenager, and you pay higher insurance premiums as a result.) Although your group, on average, may be involved in a larger number of accidents, it is possible that you as an individual are a safe and careful driver. It also is possible that a forty-year-old who is a member of a safe-driving population or group (other forty-year-olds) could be exceptionally reckless. In fact, that person might even run into you. Whom do you think a police officer on the scene of such an accident would assume was at fault? Most people accept the sharing of risk among group members when insurance is the issue. But, would it be appropriate for the officer to draw conclusions based on the average characteristics of your particular group when individual blame is the issue? This activity debates the wisdom of using statistical data based on behavioral genetics to set social policy for the entire country.

The specific behavior you will analyze is alcohol abuse. Alcohol abuse is a serious problem facing American society. In this activity, you will use what you have learned about the science of behavioral

genetics to evaluate the merits of a proposed public policy to control alcohol abuse and dependence.

Materials (per team)

- 1 copy of *Reasons in Favor of and Against Paula's Law*
- 1 copy of *Applegate Genotype Results*

Process and procedures

1. Read the following excerpt from a diary written by a college student:

Paula's diary for March 2, 2001

I remember my first drink. It was in eighth grade—my Dad let me have a beer at one of his parties. It was the first time I really felt normal. I didn't have another drink until my junior year. I've partied a lot since then. It's so easy to sneak stuff from Dad's liquor cabinet. It seems like what I'm doing with my friends isn't all that different from his parties with his friends. Last night at a fraternity party on campus, LaShawna and Kaitlin told me that they think my drinking is out of control. They say that once I start I don't stop. I told them they were nuts. But, this morning I woke up in my car in a neighborhood I didn't recognize, and I had no idea how I got there. I had to drive around for like 20 minutes until I found something I recognized. There are times when a drink is all I really want. When I think about it, maybe Dad has a drinking problem himself—and he's pretty successful. I think I might ask him about it. No, I'll call Claire. Her brother went to jail for drunk driving and she hasn't had a drink since. She should know something.

Student Pages

2. Read the following to learn what happened to Paula and how her father attempts to fight the effects of alcohol abuse.

Proposing a Change

Paula died two months later, when, under the influence of alcohol, she drove her car at high

speed into a lamppost on the freeway. Her successful father is, in fact, a United States senator. Devastated by this tragedy, he set about learning all he could about the causes of Paula's alcohol dependence. He learned, for example, that four genes influence the risk for alcohol dependence. Those genes together account for 55 percent of the

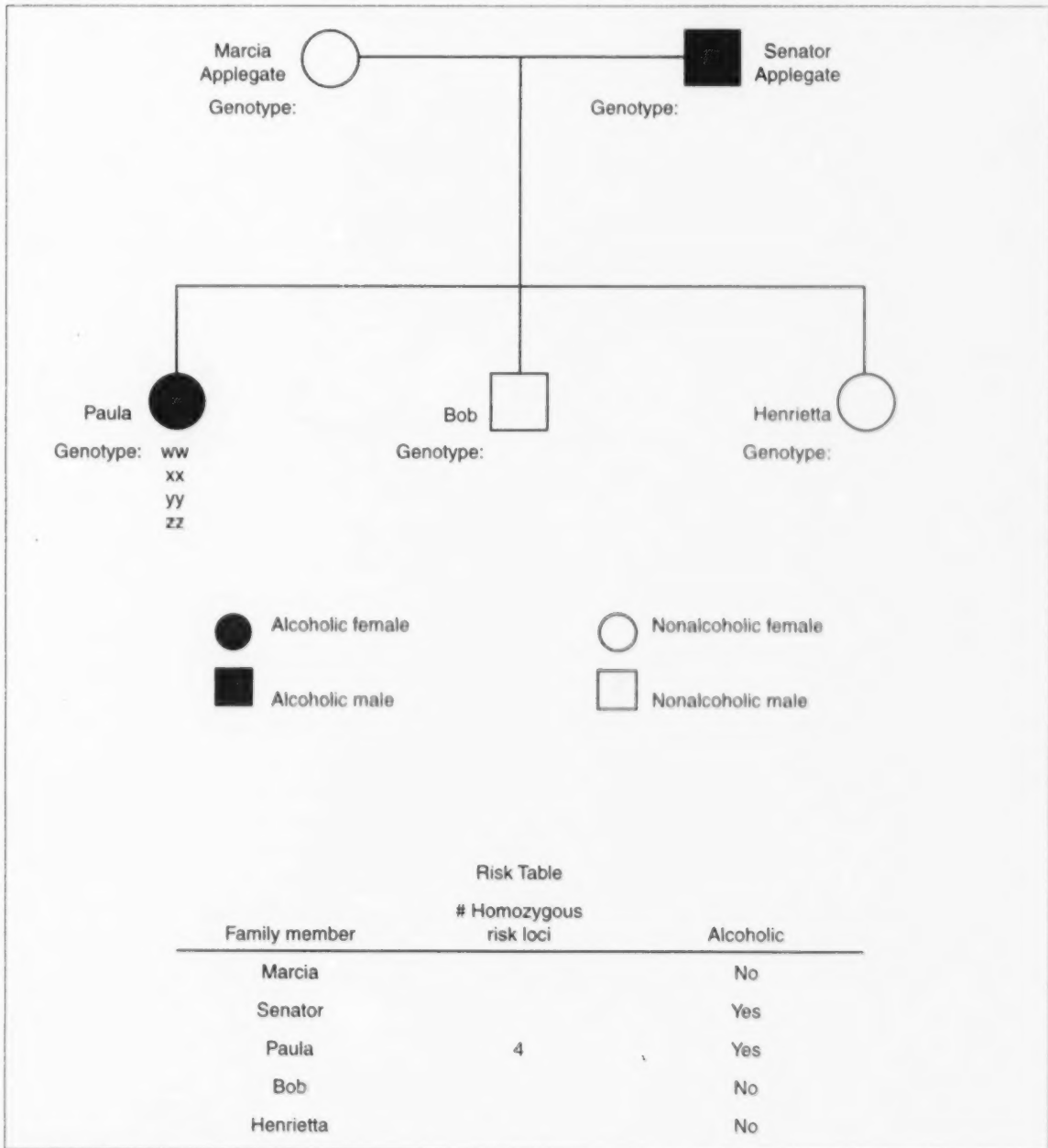


Figure 5.1 Applegate family pedigree and risk table.

total risk for alcohol dependence. (Such loci have not really been identified, but it is reasonable, based on current scientific research in this area, to think that this may happen in the next several years. Then again, this estimate may be too optimistic; even after many years of research, scientists may not be able to identify four loci with this great an effect.) Genotypes for these alleles can be determined by a simple polymerase chain reaction-based procedure, similar to the one you simulated during Activity 4, *Finding the Genes That Influence Novelty-Seeking Behavior in Humans*.

Five years after Paula's death, in the year 2006, Senator Applegate believed that the understanding of the genetics of alcohol abuse had matured enough, and that he understood the science well enough, to propose policies regulating the purchase and consumption of alcohol. On the senate floor, Senator Applegate delivered a speech arguing for his legislation, which is designed to minimize alcohol abuse.

3. Working in teams of two, use *Senator Applegate's Speech before the United States Senate* and the *Press Release on Paula's Law* to complete the chart *Reasons in Favor of and Against Paula's Law*. Be sure to consider carefully all that you have learned about behavioral genetics. At this point, do not take a personal position on the legislation.
4. Use the *Applegate Genotype Results* to complete the Applegate family pedigree and the risk table found in Figure 5.1. Answer the following:
 - a. What evidence from behavioral genetics is included or implied in Senator Applegate's legislation and press release? Is the genetic evidence fundamentally more valuable than non-genetic evidence, such as the number of driving-while-intoxicated (DWI) citations?
 - b. Where are the influences of genes acknowledged?
 - c. Where are the influences of environment acknowledged?
5. Revise the chart *Reasons in Favor of and Against Paula's Law* as necessary. Did the additional information from the completed genotype results cause you to add or delete any of your reasons? Explain.
6. What are the three most compelling reasons in favor of, and against, the proposed legislation?
7. Determine your own personal position on this legislation or argue an alternate position. Would you support Applegate's legislation? Oppose it? Are you somewhere in between those two extremes? Move to the locations in the room for each of these positions, as directed by your teacher.
8. Once at your location, explain to other students why you are standing there. Listen to the reasoning of your classmates and move to new locations as you hear compelling reasons. Only one student should speak at a time.
9. When directed by your teacher, take a class vote on the legislation and determine whether it would pass. Propose changes (amendments) to the legislation that would make it more acceptable and vote on those as time allows.

Analysis questions

1. In what ways does Senator Applegate's proposed legislation appropriately use information gained from research into behavioral genetics? In what ways is the information used inappropriately?
2. How might things have been different if Paula had grown up in a home or community where use of alcohol was prohibited and access to alcohol was impossible? In such a case, would Paula's genetic background matter? Why or why not?
3. What other actions could we take, besides using the findings from behavioral genetics, to minimize the problems associated with alcohol dependence and abuse?
4. How would you have responded if Senator Applegate had stated that a single gene had been discovered that accounts for all of the risk of alcohol dependence? Explain.

Pulling it all together

To conclude the activity and the module, pretend that the editor of your school newspaper has asked you to write a scientific evaluation of Senator Applegate's proposed legislation. Write a short article that would serve as a scientific critique of the proposed law using references to information and concepts from the activities in this module. You will be assessed on your basic writing skills, the degree to which you refer to and explain principles of behavioral genetics from the module, and the clarity and organization of the ideas you present.

Senator's Applegate's Speech before the United States Senate

My daughter Paula died five years ago. She drove her car into a lamppost on the freeway, and she was drunk when she did it. I'll never know if it was suicide or an accident, but I go to bed every night wondering whether I could have saved my daughter. What I do know now, from what her friends have told me, is that she clearly abused alcohol throughout her last few years of high school and in college.

I have proposed legislation to create a new government program, to be called the **Alcohol Freedom Program**, that will prevent tragedies involving alcohol. The program will be fully funded by a new sales tax on beverage alcohol. Informally, I think of this legislation as "Paula's Law." Please refer to the accompanying press release for details about the science underlying this proposal.

SENATE BILL S106

THIS LEGISLATION WILL REQUIRE EVERY PERSON WHO WISHES TO PURCHASE ALCOHOLIC BEVERAGES TO OBTAIN AN ALCOHOL FREEDOM CARD, WHICH MUST BE PRESENTED AT THE TIME OF ANY PURCHASE OF BEVERAGE ALCOHOL. THE LEGISLATION HAS SIX BASIC PROVISIONS:

1. EVERY PERSON CURRENTLY 18 YEARS OF AGE OR OLDER WILL PROVIDE A SAMPLE OF CHEEK CELLS. DNA WILL BE EXTRACTED. GENOTYPES AT EACH OF FOUR RELEVANT LOCI WILL BE DETERMINED AT A NEWLY CREATED GOVERNMENT LABORATORY. THE GENOTYPES WILL BE ENTERED INTO A NATIONAL DATABASE.
2. UPON REACHING THE AGE OF 21, A PERSON MAY REQUEST AN ALCOHOL FREEDOM CARD. THESE CARDS WILL CONTAIN AN INDIVIDUAL'S GENOTYPE AT THE ALCOHOL-DEPENDENCE RISK LOCI. THE ALCOHOL FREEDOM CARD WILL BE REQUIRED TO PURCHASE BEVERAGE ALCOHOL.
3. THIS LEGISLATION ALSO WILL CREATE A SECOND DATABASE, TO BE CALLED THE ALCOHOL PURCHASE REGISTRY. AT THE TIME OF EACH ALCOHOL PURCHASE, THE ALCOHOL FREEDOM CARD WILL BE SWIPED AND THE DATABASE ACCESSED. THE DATABASE WILL RECORD EACH INDIVIDUAL'S BEVERAGE-ALCOHOL PURCHASES MADE WITH THE ALCOHOL FREEDOM CARD. IN ADDITION, THE DATABASE WILL BE PROGRAMMED TO IDENTIFY ALL INDIVIDUALS WHO PURCHASE EXCESSIVE AMOUNTS OF BEVERAGE ALCOHOL.
4. BEVERAGE ALCOHOL PURCHASES WILL BE PROHIBITED UNDER EITHER OF THE FOLLOWING CONDITIONS:
 - A. INDIVIDUALS WITH ALL FOUR SUSCEPTIBILITY ALLELES WILL BE DENIED THE PRIVILEGE OF PURCHASING ALCOHOL.
 - B. INDIVIDUALS WITH A RECORD OF EXCESSIVE BEVERAGE-ALCOHOL PURCHASES WILL BE DENIED THE PRIVILEGE OF FURTHER ALCOHOL PURCHASES.
5. PENALTIES FOR ILLEGAL SALE OR TRANSFER OF ALCOHOLIC BEVERAGES WILL BE ESTABLISHED AND WILL INCLUDE FINES AND IMPRISONMENT.
6. APPROPRIATE EXCEPTIONS WILL BE ALLOWED FOR RELIGIOUS AND CERTAIN OTHER USAGES, CONSISTENT WITH THE FIRST AMENDMENT.

Friends, I have been so impressed by the power of these genetic methods that I had a sample of my daughter's blood tested for the four loci in the proposed legislation. Sure enough, she had all four genetic risk factors. If Paula had had this genetic test while still alive, the proposed legislation would have prevented her from getting within one hundred yards of a drink. Had she known of her risk, she would have been influenced by her own prudence to avoid alcohol, and had I known, I would have taken steps to rid our house of alcohol. Also, if her high level of alcohol purchases after the age of 21 had been monitored by the government, action could have been taken to prevent further excess purchase and consumption.

We now have the opportunity to apply important scientific information to the benefit of all of our citizens, young and old alike. I urge you to support this landmark legislation. There is absolutely no doubt that this law will save lives—at a cost of only a small loss of individual liberty. Think of my daughter, and realize that the first life saved under this legislation might be yours—or, more importantly, that of your child.

Press Release on Paula's Law

From the Office of Senator Otis Applegate
The Capitol, Washington, D.C., USA

Alcohol Abuse and Motor Vehicle Accidents

- Approximately 45,000 people die in motor vehicle accidents each year.
- Of all fatal motor vehicle accidents, alcohol is involved about 35 percent of the time.
- Approximately 30 percent of those killed in alcohol-related motor vehicle accidents are between the ages of 16 and 24.

Family and Twin Studies

- About 13 percent of Americans have a problem with alcohol dependence. Thus, alcohol abuse is a prevalent problem in our society.
- Several studies have shown that the biological children of alcohol-dependent subjects are at increased risk for developing alcohol problems themselves.
- The adopted children of alcoholics develop drinking problems at a higher rate than the adopted children of nonalcoholics.
- Twin studies have shown that monozygotic, or identical, twins are more likely to share the diagnosis of alcohol dependence than dizygotic or fraternal twins.

Genetic Studies

- Genes coding for enzymes that metabolize alcohol affect the risk for alcohol dependence. For example, in some Asian populations, polymorphisms in these genes can result in the buildup of a somewhat toxic metabolite of alcohol in the blood. People with alleles resulting in a greater buildup of the toxic metabolite tend to feel a little sick when they drink. As a result, they are at lower risk for developing alcohol dependence.
- Two extensive studies published in the late 1990s detected the presence of other genes influencing risk for alcohol dependence. However, those studies did not actually pinpoint the location of the genes or establish their function. Now, in 2006, some of the genes located in those studies have been identified.
- Four specific genes increased the risk for alcohol dependence in one population study. Each gene operates in recessive fashion, so risk is associated only with homozygotes. Although this research involved only a limited number of participants, the scientists estimate that, together, these genes might account for 55 percent of the risk for alcoholism in this disorder.

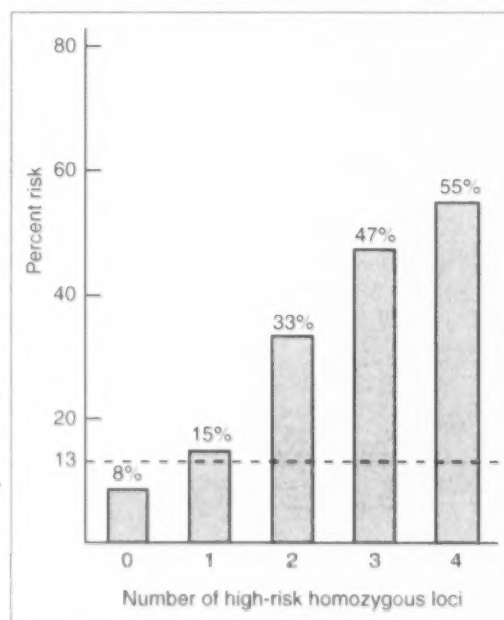


Figure 5.2 Risk for alcoholism by genotype.

Policy Implications

Identifying predispositions

a. There is now the potential for:

- identifying the physiological basis of the disorder;
- developing new treatments;
- preventing onset of illness; and
- identifying individuals with genetic predispositions to alcohol abuse and, consequently, those who may exhibit behaviors detrimental to our society.

Student Pages

- b. If we can identify at-risk individuals, we may be able to prevent those unwanted behaviors *before they appear*. The degree to which we will ever be able to prevent the behavior will depend on the predictive value of the genetic test.
- c. We know a great deal about the behavioral aspects of alcohol dependence and the contribution of environmental factors to alcohol dependence. Combining that knowledge can provide powerful predictions of future risk for alcohol dependence.

Government regulation

- a. Paula's Law proposes a level of government interference in the behaviors of the American people that is already accepted.
 - Government control over alcohol is well established.
 - Government control over access to drugs other than alcohol, such as marijuana, cocaine, and heroin, is even greater.
 - State and local regulation has existed for many years. For example, the state of Oregon issues a separate identity card that must be used to purchase alcohol. In Texas and many other states, counties have the legal power to ban the purchase of hard liquor within their jurisdiction and many do so.
- b. Large databases exist in many places.
 - The government tracks handgun sales as part of the Brady Law and maintains those data in a national database.
 - Many grocery stores swipe store cards in check-out lines and track the individual purchases of their customers.



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